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President's message

Dear colleagues,

Warm regards to you.

April-May is the festival season, Christians celebrated Easter,the festival of new hope, Hindus celebrated Vishu, the auspicious first day of the New Year. Muslims will be celebrating the Eid to mark the end of Ramadan, the holy month of fasting. But this year all of them were lackluster events, thanks to Covid 19.

The devastating effects of the first wave of Covid itself were terrifying. The economic fallout of the pandemic is yet to set in. Numerous small business establishments around us were closed down and many lost jobs. The boarder issues with the neighboring countries and the resultant import restrictions from China is affecting the dental profession dearly. We were highly dependent on China for equipments and materials. Now the new products as well as the spares are not available in the market. Even the equipments with warranty won't be serviced.

The availability of cheap material supplies from China was keeping the prices down for disposables like Gloves Masks etc. As that supplies dried up the prices skyrocketed. In addition to that the practitioners are spending extra for fumigations and additional protective gears. It is judicious to pass on these additional expenses to the patients. It's a fact that the number of cases in every clinic has come down, but it's a transient phenomenon and once this calamity is over things will get back to normal.

My accountant friends are of the opinion that doctors are good in generating income but most of them don't know the proper money management, so as to make the money work for them. In these times of generalized economic slowdown, we should be more prudent in managing our resources. Dentistry as such is not considered as an emergency in our community and the expensive periodontal therapy always take a back seat. So the upcoming months are going to be meek as we are going to get exposed to the wrath of the second wave of Covid. Early reports show a much more damaging episode than the first one.

I hope everyone had their vaccination by now. Even with that I urge all of you to continue your vigil in the clinic as well as in the social circles, hope this will settle in few months time.

Thank you.

Dr Sabu Kurian
President, SPIK

Secretary's Message

Dear colleagues of the SPIK fraternity,

Periodontics as a specialty is growing in relevance day by day worldwide especially as its significance and role in Implant dentistry are becoming more and more evident. As Periodontists, no one is placed at a better position to maintain the perfect balance between preserving the natural whenever possible and providing the perfect alternative elsewhere. However, the challenge of disseminating periodontal awareness in the society still remains. SPIK, representing majority of the Periodontists in the state, has the prime responsibility in the above.

The current office has been severely restrained by the COVID scenario in conducting most of our regular events. Considering this, the extra-ordinary general body meeting of SPIK held online on 30-01-2021, proposed to extend the term of the office for one more year. We thank the SPIK members for this opportunity and hope to resume our activities at the earliest as the situation permits.

As always, our editor, Dr. Sameera G. Nath is continuing her laudable performance as the Hon. Editor of JSPIK. It is my humble plea to all members to contribute to our journal. We are also exploring the possibility of getting JSPIK indexed in one of the standard indexing databases so that it gets a wider acceptance among the periodontal fraternity.

While I am writing this, we yet are to get out of the roller coaster ride set forth by the COVID pandemic. History tells us that this is likely to continue for a while. Let us be patient and continue to observe our vigil. As Desmond Tutu said, "hope is being able to see that there is light despite all of the darkness".

Dr. Jayan Jacob Mathew
Secretary, SPIK

INFORMATION TO AUTHORS

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Estimation of the knowledge and awareness of Gynecologists regarding gingival / periodontal diseases during pregnancy – A cross-sectional study

Krishnapriya S.[1], Jose Paul[2], Johnson Prakash D'Lima[3], Senny Thomas Parackal[3], Deepak Thomas[4], Jenny Susan Roy[5]

ABSTRACT

Background: Gynecologists are the primary health care professionals in direct contact with pregnant women. Understanding the extent of their awareness about the relationship of periodontal disease with the outcomes of pregnancy will enhance pregnancy outcomes and avoid preterm delivery.

Aim: The study was conducted to evaluate the knowledge and awareness of Gynecologists regarding oral health care during pregnancy and the association of periodontal disease with adverse pregnancy outcomes.

Methods: A structured questionnaire consisting of nine questions was administered to 100 Gynecologists practicing in different parts of Kerala.

Results: Among the 100 participants, 97% acknowledged a connection between oral health and pregnancy and 62.5% agreed that periodontal disease can affect the outcome of pregnancy. 64% of them had patients who reported with bleeding gums or tooth mobility during pregnancy. 88% of them suggested that second trimester is the safest for provision of dental treatment.

Conclusion: The present study demonstrated that Gynecologists have a relatively high degree of knowledge with respect to the relationship of periodontal disease to pregnancy outcome. However, there clearly exist misconceptions regarding the provision of dental treatment during pregnancy. To provide better oral health care, more knowledge needs to be made available to the pregnant women and the medical community.

KEY WORDS: gynecologist, preterm and low birth weight, periodontal disease, pregnancy

Introduction

Pregnancy entails complex physiological and hormonal changes that influence almost every organ system including the oral cavity.[1] The hormones estrogen and progesterone increase during pregnancy, which have been found to affect the development of periodontal disease and wound healing, also lead to increased gingival vascularisation and reduced immune response.[2] Pregnancy-related oral disorders mainly include gingivitis and periodontal infection.[2] Specific risk factors like maternal age, socioeconomic status, nutritional status, stress, interval of birth, maternal hypertension, infection and cervical incompetence have shown an increased risk of PTLBW (preterm and low birth weight).[2] The American Academy of Periodontology suggested periodontal evaluation and appropriate care for pregnant women and people who are preparing for pregnancy.[3-5] Meta-analysis of randomized controlled trials suggested that periodontal treatment during pregnancy reduces the risk of PTLBW.[5] Research found that 18.2% of all cases of PTLBW can be linked to periodontal diseases.[6] The mechanisms by which periodontal diseases may

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cause premature birth and or low birth weight was not clarified.

Maternal infection can lead to the presence of amniotic bacterial products such as lipopolysaccharides from gram negative organism, which stimulates the development of host derived cytokines in the amnion and decidua. These cytokines, including 1L.-I, TNF-α and IL-6, stimulate increased prostaglandin production from the amnion and decidua, leading to onset of preterm labor.[7] Jeffcoat et al., observed a reduced risk of premature birth rate in women who received mechanical periodontal care during gestation.[8] Gynecologists are the primary health care professionals in direct contact with pregnant women. Understanding the extent of their awareness about the relationship of periodontal disease with the outcomes of pregnancy will enhance pregnancy outcomes and avoid premature delivery. There are very few longitudinal research and studies conducted to assess the association between periodontitis and adverse pregnancy outcome.

Knowledge of gynecologists about gingival/periodontal infection during pregnancy

1. Do you agree that pregnancy increases the likelihood of gingival inflammation?
YES ☐ NO ☐

2. Do you think that there is a possible connection between the health of theteeth and gum and pregnancy?
YES ☐ NO ☐

3. Do you believe that gingival/periodontal inflammation can affect the outcome of pregnancy?
YES ☐ NO ☐

4. Do you think periodontal disease can lead to preterm labor and/or low birth weight?
YES ☐ NO ☐

5. Do you advise patients to visit dentist during pregnancy
YES ☐ NO ☐

6. Do you advise patient to delay visit to the dentist until after pregnancy
YES ☐ NO ☐

7. Local anesthesia with vasoconstrictors in pregnancy is safe
YES ☐ NO ☐

8. Safest trimester of pregnancy for provision of dental treatment
First trimester ☐ Second trimester ☐ Third trimester ☐

9. Have your patients reported with bleeding gums or tooth mobility during pregnancy?
YES ☐ NO ☐

Figure I: Questionnaire

The goal of this study was to assess Gynecologist's information, understanding and practice behaviors regarding oral health care during pregnancy and the correlation of periodontal disease with adverse outcomes of pregnancy.

Materials and Methods

A cross-sectional study was conducted among 100 Gynecologists belonging to different parts of the state of Kerala, India. A Questionnaire containing 9 questions, consisting of 8 close ended questions and one multiple choice questions relevant for this study were selected from similar published study[9]. The questionnaire was distributed among 100 Gynecologists who consented to participate in the study.[9] The principal investigator directly approached the gynecologists and circulated the questionnaire after receiving their verbal consent. Their confidentiality was assured. All the Gynecologists who enrolled for the program filled all the questions in the questionnaire in approximately 5 minutes. The following were the questions in the questionnaire (Figure 1).

Statistical analysis

All returned questionnaires were recorded and analyzed. Results were expressed as the number. Score 1 was assigned for positive response and score 0 for a negative response. Here Chi-square test was used to evaluate the difference between the variables, and the level of significance was set at $p < 0.05$. For statistical analysis we used SPSS version 24.

Results

All the Gynecologists who agreed to participate in this study returned completely filled questionnaires, yielding a response rate of 100%. Table I displays the responses of the Gynecologists to the questions aimed to evaluate their knowledge regarding the association between oral health and pregnancy. 96% of the participants agreed that pregnancy increases the likelihood of gingival Inflammation. 98% believe that there is a positive correlation between the health of the gum and pregnancy. About 66% of Gynecologists agree that periodontal disease can lead to preterm labor and/ or low birth weight. 52% of the Gynecologist advice their patients to visit dentist during pregnancy and 40% insist their patient to delay visit to the dentist

until after pregnancy.

38% consider that dental treatments with the administration of local anesthetics are safe during pregnancy. The study showed that 88% were aware that second trimester is the safest to provide dental treatment. 68% of the surveyed Gynecologists reported that their patients mentioned about bleeding gums or tooth mobility during pregnancy. Since the p value > 0.05, the results of the study came out to be statistically non significant.

Discussion

This study was conducted to determine the Gynecologist's level of knowledge about the correlation of periodontal disease and the outcome of pregnancy. Overall result from this survey reflect the knowledge of Gynecologists with most of the oral problems associated with pregnancy, but there is still some misunderstanding about receiving dental care during pregnancy. This is critical for the dentists because it acts as an obstacle to provide their pregnant patients with the most effective dental care. Especially regarding administration of local anesthetic, only 38% consider that dental treatments with the administration of local anesthetics as safe during pregnancy. Vasoconstrictors increase the duration of anesthesia and ensure that pain is managed effectively during dental treatment. Pain-free dental care is important, as pain raises stress levels and also induces hormonal changes that can be detrimental to pregnant patients.[9]

Research has shown that the use of regular dental anesthetics containing vasoconstrictors during pregnancy is safe, provided intravascular injections are avoided.[10] In the anesthetic solution, the vasoconstrictors are present in a very small quantity and thus pose no danger to the fetus or to the pregnancy itself. From this study it is clear that almost 97% of Gynecologists are aware regarding the association between pregnancy and oral health problem, but only 50% of them advice their patients to visit dentist. About 65% of Gynecologists were aware of the importance of providing adequate dental treatment during pregnancy.

Table I: Knowledge of Gynecologist about gingival/ periodontal health during pregnancy

Knowledge statement	*Number of participants with positive response*	*Advised visiting the dentist*	*Did not advise visiting the dentist*	*P value*
Pregnancy increases the likelihood of gingival inflammation	96	50	46	0.935
There is a possible **c**onnection between the health of the teeth and gum and pregnancy	98	52	46	0.137
Gingival/periodontal inflammation can affect the outcome of pregnancy	61	34	27	0.349
Periodontal disease can lead to preterm labor and/or low birth weight	64	35	29	0.473
Do you advise patient to delay visit to the dentist until after pregnancy	39	19	20	0.599
Local anesthesia with vasoconstrictors in pregnancy is safe	35	22	13	0.111
Have your patients reported with bleeding gums or tooth mobility during pregnancy	64	37	27	0.121

About 68% of the participated Gynecologists had patients reported with bleeding gums, and 40% of them advice their patient to delay visit to dentist until the pregnancy is over.

Seventy eight percentage know that second trimester is the safest to provide dental treatment without any harm. Owing to the morning sickness encountered by most pregnant women during the first trimester and the high risk of postural hypotension during the third trimester, the optimal time for efficient dental treatment is the second trimester of pregnancy[11, 12]. The hormonal changes taking place during pregnancy render the women more susceptible to plaque accumulation and gingival inflammation[13]. Likewise, any acute periodontal infection should be treated as soon as possible to avoid harm to the mother and the developing fetus[14, 15].

Study conducted by Hashimet al[9] among Gynecologists in UAE displays similar results with some exception. In their study they found that about 85.2% advised their pregnant patients to visit the Dentist, but in this study only 52% advised their pregnant patients to visit the dentist during pregnancy. A very high percentage (93.5%) of the Gynecologists in their study reported that their patients mentioned bleeding gums or tooth mobility during pregnancy, but in this study only 64% reported that their patients complained of bleeding gums or tooth mobility during pregnancy.

To our knowledge, this is the first study conducted in Kerala to determine the Gynecologist's level of knowledge regarding the relationship between periodontal disease and pregnancy outcomes. Insufficient sample size may be a limitation of the study to provide definitive conclusions on the matter. Nevertheless, the obtained responses did not necessarily reflect the actual opinions of the participating Gynecologists due to bias on their part. Moreover, the real oral health status of the pregnant women who visited these Gynecologists could not be measured and it was focused solely on the participating Gynecologist's recollection.

Figure II: Graphical representation of responses regarding safest trimester for provision of dental treatment

This study might provide potential reference knowledge for continuing education programs in future that are provided to Gynecologists with additional information regarding the association between periodontal disease and adverse pregnancy outcomes. It is suggested that Gynecologists should be educated on how to include visual screening for oral health problems during their examination of pregnant women. Also, it will be useful to have an oral health referral sources available for Gynecologists so that pregnant women can be conveniently referred to for oral health needs.

Conclusion

Gynecologists are the core members who can detect oral health problem in pregnancy. Adequate knowledge of Gynecologists regarding the oral health problem encountered during pregnancy and the importance of treating the same can improve the oral health status, and wellbeing of pregnant women as well as the new born. Gynecologists in this study displayed certain level of knowledge, but misconceptions exist among some of them regarding the types of dental treatment performed during pregnancy and its importance. So in order to have a better pregnancy and good pregnancy outcome, more awareness and knowledge needs to be made available to the pregnant women and medical community, mainly to the Gynecologists who are primary health-care providers.

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Obesity and Periodontal Disease

Sruthy Madhusudanan[1], Ambili R[2], Seba Abraham[2], Arunima P R[2], Reejamol R[3]

ABSTRACT

Excessive fat deposition in adipose tissue leads to obesity, which is a common health problem today. Obesity can lead to adverse metabolic effects on health which leads to elevation in oxidative stress causing endothelial dysfunction and an increase in proinflammatory cytokines leading to periodontitis. The association between obesity and periodontitis is yet to be defined through studies, but the variety of cytokines and hormones like lectin, adiponectin, resistin and visfatin are released by the adipose tissue that are involved in various inflammatory processes. This points towards the similar pathways involved in the pathogenesis of obesity, periodontitis and other inflammatory diseases. So the aim of this article is to provide an overview of the association between obesity and periodontitis.

KEY WORDS: obesity, adipokines, periodontitis.

Introduction

One of the major health problems today is obesity, which is defined as a body mass index (BMI) >30.0 kg/m^2. Various health consequences like diabetes mellitus, hypertension, heart disease like coronary artery disease, heart failure, dyslipidemia, hemorrhagic and ischemic stroke, pulmonary abnormalities like obstructive sleep apnea, asthma, gastrointestinal diseases like gastroesophageal reflux disease, cholelithiasis, osteoarthritis, reproductive disease like polycystic ovary syndrome in females and impotence and infertility in males, cancer of gallbladder, esophagus (adenocarcinoma), thyroid, kidney, uterus, colon and breast, and Psychosocial problems are associated with obesity.[1] Recent studies have suggested that obesity is also associated with oral diseases, particularly periodontitis.[2] Several cytokines and hormones are secreted from adipose tissue that are involved in inflammatory processes, suggesting that similar processes may be involved in the pathophysiology of obesity and periodontitis. This evidence-based review is an attempt to provide an overview regarding obesity and its possible association with periodontal disease.

Prevalence of obesity

Obesity in adults and overweight in children had markedly increased as per the reports ofNational Health and Nutrition Examination Survey III (1989-1991). Those trends continued such that approximately 31% of American adults now meet the criteria for obesity. More than 65% of the United States adult population has a body mass index of ≥25 kg/m^2, and 15.8% of children aged 6-11 years and 16.1% of adolescents aged 12-19 years are overweight. Prevalence of obesity among adults has doubled, and the prevalence of overweight among children and adolescents has tripled during this short period of time.[3] In India, more than 135 million individuals were affected by obesity. It's prevalent in all category of people with varying age, gender, geographical environment, socio-economic

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status, etc. According to ICMR-INDIAB study 2015, prevalence rate of obesity and central obesity varies from 11.8% to 31.3% and 16.9%–36.3% respectively. Abdominal obesity is one of the major risk factors for cardiovascular disease in India. (CVDs).[4]

Classification of overweight and obesity

Excess visceral fat or central obesity has been shown to have a strong association with cardiovascular disease compared to subcutaneous fat (mainly deposited around the hips and buttocks). Waist Circumference (WC) is used to measure the body fat distribution, the cut off point for abdominal obesity in men is 102 cm and in women is 88 cm. Waist circumference shows a close correlation with the amount of visceral adipose tissue. Visceral adipose tissue is metabolically more active and secrete far greater amounts of cytokines and hormones compared with subcutaneous adipose tissue.[5] Recent studies have indicated that measurement of waist circumference or waist-hip ratio may be a better disease risk predictor than BMI, and there is still intensive research ongoing as to whether BMI, waist circumference or both should be used to assess disease risk.[6,7]

Association between obesity and periodontitis

Obesity is suggested as the second only to smoking strongest risk factor for inflammatory periodontal tissue destruction.[10] The first report on the relationship between obesity and periodontal disease appeared in 1977, when Perlstein et al. observed histopathologic changes in the periodontium in hereditary obese Zucker rats. Using ligature-induced periodontitis, they found alveolar bone resorption to be greater in obese animals compared with non-obese rats. Also, it seemed that under healthy oral conditions, obesity per se does not promote pathologic periodontal alterations; however, in response to bacterial plaque accumulation, periodontal inflammation and destruction were more severe in obese animals.[2] Later on, the hypothesis of obesity as a risk factor for periodontal disease was supported by epidemiological studies.[3]

A variety of potential mechanisms could explain the association between obesity and periodontitis. The two important mechanisms include Biological and Health risk behavior mechanism

I. Biological mechanism:

Fat tissue is not merely a passive triglyceride reservoir of the body, but also produces a vast amount of cytokines and hormones, collectively called adipokines or adipocytokines, which in turn may modulate periodontitis[11] and play a key role in the association of obesity and periodontal diseases. The important adipokines in periodontal disease are discussed below.

1. Leptin

Leptin is a pleotropic cytokine secreted by adipocytes. It has a role in a variety of biological processes, like energy metabolism, endocrine functions, reproduction and immunity. Leptin act as a "lipostat" that regulates adipose tissue mass. As a negative feedback mechanism, increase in level of leptin concentrations may lead to an increase in energy expenditure,

Table 1: Classification of obesity based on expert panel 1998[8]

Disease risk relative to normal weight circumference and waist			
Classification	**BMI (kg/m^2)**	**Men < 102cm Women < 88cm**	**Men >102cm Women > 88cm**
Underweight	<18.5	-	-
Normal	18.5 – 24.9	-	-
Overweight	25 – 29.9	Increased	High
Obese Class I	30 – 34.9	High	Very High
Obese Class II	35 – 39.9	Very High	Very High
Obese Class III	>40	Extremely High	Extremely High

decreased food intake and a negative energy balance. But at the receptor level overweight and obese persons may show a resistance to leptin and thus have elevated leptin levels than non-obese individuals.[12] Leptin has also a role in bone metabolism. Although the data appear controversial, evidence has suggested that leptin may decrease bone formation through central nervous pathway, and it may stimulate bone formation via direct peripheral effects on bone cells. General and bone-specific factors, such as species, age, gender, serum leptin levels, blood-brain barrier permeability, bone tissue, skeletal maturity and signaling pathways are dependent on the net result of bone formation.[13] In periodontal disease, leptin regulation has still to be examined, especially with respect to the epidemiological association between obesity and periodontitis. One study implied decreasing leptin levels in gingival biopsies with increasing pocket-probing depths, which would be contrary to the cited data on other inflammatory diseases.[14] Leptin as a pleotropic adipokine has a role in bone metabolism and causes alveolar bone destruction in periodontitis.[15]

Table 2: Classification of obesity based on International classification of body mass index (Adapted from WHO, 20089)

Classification	Body mass index (kg/m_2)	
	Principal cut off points	Additional cut off points
Underweight	<18.50	<18.50
Severe thinness	<16	<16
Moderate thinness	16.00 – 16.99	16.00 – 16.99
Mild thinness	17.00 -18.49	17.00 -18.49
Normal range	18.50- 24.99	18.50 – 23.99 24.00 – 24.99
Overweight	≥25.00	
Pre obese	25.00 – 29.99	25.00 – 27.49 27.50 – 29.99
Obese	≥30.00	
Obese class I	30.00 – 34.99	30.00 – 32.49 32.50 – 34.99
Obese class II	35.00 – 39.99	35.00 – 37.49 37.50 – 39.99
Obese class III	≥40.00	≥40.00

2. Adiponectin

Adiponectin secreted by adipose tissue has a role in glucose and lipid metabolism and it is a circulating hormone. It consists of 0.05% of total serum proteins. This level is reduced in persons with obesity, insulin resistance or type 2 diabetes. Adiponectin improves insulin sensitivity and it have anti-atherogenic and anti-inflammatory properties. Low plasma adiponectin levels are found in type 2 diabetes and coronary heart disease in humans.[16] But low adiponectin levels are not related to periodontal diseases[17] and it was suggested that treatment with antimicrobial periodontal therapy will not have an increase in adiponectin levels.[18] Adiponectin inhibit monocyte adhesion to endothelial cells and macrophage transformation to foam cells.[19] It also appears to be important in bacterial and viral infections. It was shown to negatively regulate mouse macrophage-like cell responses to Toll-like receptor (TLR) ligands.[20] It also has a role in inhibition of osteoclast formation which was stimulated by LPS from periodontopathic bacteria.[21] Thus, collectively these observations came to conclusion that adiponectin may inhibit alveolar bone loss in periodontitis. Thus stimulation with adiponectin enhances the regenerative and proliferative capacity of the periodontal tissues.[22]

3. Resistin

It belongs to a family of resistin-like molecules (RELM), secreted by adipocytes and they cause insulin resistance in animal models. However, studies have shown that the role of resistin differs between species, and many aspects, specifically its association with obesity and its effects on insulin sensitivity in humans, remain controversial. Current studies have suggested that, resistin is more closely related to inflammatory processes than to insulin resistance in humans. Whether or not resistin plays a role in inflammatory periodontal disease remains to be defined.[23] Adipose-tissue–derived cytokines and hormones are being discovered, the endocrine network of which these mediators are a part becomes clearer. There are few studies related to the association between resistin and periodontitis. In a study conducted by Furugen et al reported that the serum resistin levels is increased in chronic periodontitis patients compared with the

non-periodontitis patient.[24] Another study done by Zimmermann et al. who conducted study in determining the serum and GCF levels of adipokines in obese and non obese subjects, with and without chronic periodontitis. It was concluded that the level of resistin was increased while adiponectin levels was decreased in periodontitis group compared to the non-periodontitis groups. Thus the authors came to a conclusion that periodontitis influences the circulating levels of resistin and adiponectin.[25]

4. Visfatin

Recent discovery to adipokines include visfatin, which elicits insulin-like effects. Visfatin, exerts hypoglycaemic effect by binding to insulin receptor at a site distinct from insulin. In inflammatory conditions like periodontitis the levels of visfatin is increased. A study done by Tabari et al. concluded that there is significant increase in the concentration of salivary visfatin level in patients with chronic periodontitis.[26] In another study conducted by Özcanet al[27] who concluded that there is an increased levels of visfatin which is associated with the expression of NF-κB and PI3k, and this may play a role in the pathogenesis of periodontitis. Thus Visfatin may be considered as an inflammatory marker and can be used in future as a potential therapeutic target in the treatment of periodontal disease. In a study conducted by Mishara concluded that levels of visfatin are elevated in individuals with both periodontal disease and diabetes, even after periodontal therapy.[28]

In addition to above mentioned adipokines visceral fat also enhances the expression of Plasminogen activator inhibitor-I (PAl- I) that decrease blood flow in the Periodontium to promote the development of periodontitis. Obesity triggers immune response generating a chronic subclinical systemic inflammation. Adipocytes actively produce cytokines including tumor necrosis factor α (TNF-α), IL-6, and to some degree IL-1 which stimulate acute immune response in liver to produce C-reactive protein and fibrinogen. Increase in the apoptosis of pancreatic β cells caused by fat will generate immune response. This immune response interferes with glucose transporters, thus inhibiting insulin signaling causing the body to develop an inflammatory state. Studies has shown a significant association between periodontitis and serum levels of Aspartate transaminase (AST), alkaline phosphatase (ALT), cholinesterase, and AST-to-ALT ratio, suggesting that subjects with periodontitis also tend to have hepatic steatosis. Visceral fat which leads to hepatic steatosis, may also increase the risk of periodontitis.

II. Health Risk Behavior mechanism:

This mechanism involves various dietary patterns associated with the patient leading to periodontal diseases including

• Unhealthy dietary patterns with insufficient micronutrient increasing the risk for periodontal disease. Poor dietary patterns may affect oral tissues and the immune response.

• Psychosocial stress associated with overweight may affect periodontal health through physiological and behavioral pathways. (Alter blood and salivary flow, decreasing the immune response, affect oral health behaviors)

Future implications in dental practice

Until recently, a definite diagnosis of obesity was only rarely made by physicians, and body weight or body height was rarely measured in clinical practice. Further, it has been shown that about 25% of obese persons have been misclassified, by subjective estimation of the physician, as having normal weight. In future, if obesity is to be acknowledged as a multiple-risk-factor syndrome for overall and oral health, general and oral risk assessment in the dental office should include the evaluation of body mass index on a regular basis. Although there is still research ongoing as to whether BMI or waist circumference or both are a better disease risk predictor, the assessment of waist circumference in addition to BMI seems advisable, based on current obesity guidelines. Besides the suggested association between periodontal disease and obesity, periodontists need to be aware of the potential health problems related to obesity and should take them into account during risk modification.[29]

It has been suggested that supine patient positioning should be avoided, to maximize the pulmonary mechanics. Impaired chest expansion decreases vital capacity and tidal function, which compromises tissue oxygenation. These conditions put the obese person at high anesthetic and surgical risk. Wound-healing

processes are dependent on enough tissue oxygenation. Also, higher incidences of infections and post-surgical hematoma formation have been reported among obese persons. The vulnerability to wound complications increases morbidity and mortality of obese persons. Also, a close collaboration with the general physician and the dietician may be beneficial to ensure effective periodontal treatment outcome.[29]

Conclusion

Obesity is the major risk factor of various overall and oral health problems and this has been identified in various researches in recent years. Periodontists must be aware of the increasing numbers of obese persons and its significance in periodontal disease. Proinflammatory cytokines is considered as the multidirectional link between periodontitis, obesity and other chronic diseases. The adipose tissue is a large reservoir of biologically active mediators, such as TNF-α and other adipokines. Adipokines such as leptin, resistin and adiponectin are closely related to the in inflammatory processes. But their role in periodontal diseases has yet to be identified. Although this needs further investigation, periodontists should counsel obese persons regarding the oral complications of obesity, to diminish morbidity for these individuals. Thus, on a regular basis in our practice we should include the measurement of body mass index and waist circumference for periodontal risk assessment and necessary steps should be taken to manage obesity as a periodontal risk reduction strategy.

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Convergent association between Polycystic Ovarian Syndrome and Periodontal disease - A review

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ABSTRACT

Polycystic Ovarian Syndrome (PCOS) is the most common endocrine disorder among women of reproductive age, which negatively affects various health systems. There is an extensive literature regarding the association of PCOS and other systemic conditions such as diabetes mellitus, cardiovascular disease, and psychological disorders. Polycystic Ovarian Syndrome (PCOS) has reproductive and metabolic properties that may be linked to periodontitis (PD). However, there is a lack of literature in associating PCOS and periodontal disease. This literature review is on the pathophysiological mechanisms linking PCOS and periodontal diseases.

Key words: Polycystic ovarian syndrome, periodontal diseases, pathophysiology, bidirectional relationship.

Introduction

Polycystic Ovarian Syndrome (PCOS) is a complex endocrine, reproductive and metabolic condition, with a worldwide prevalence ranging 5–15%. PCOS is characterized by polycystic ovaries, hyperandrogenism with impaired gonadotropin secretory activity, hyperinsulinemia, hypothalamic–pituitary–ovarian (HPO) axis changes, and ovulatory and menstrual dysfunction. Additionally, PCOS is also accompanied by psychological alterations, such as anxiety, depression and poor quality of life. Patients with this syndrome are at higher risk of developing insulin resistance (IR), obesity, dyslipidemia, cardiovascular disease (CVD), and endometrial carcinoma.[1] IR and hyperinsulinemia are responsible for the low-grade chronic systemic inflammation. Over the last decades few cross-sectional evidence has suggested that PCOS patients may be more prone to develop periodontitis.[2]

Periodontitis (PD) is a chronic multifactorial inflammatory condition caused by a dysbiotic plaque and causes the destruction of the periodontium, the tissues that surround teeth. Periodontitis is a pandemic noncommunicable disease and its symptoms start with gum inflammation (gingivitis) to an exacerbated and uncontrolled inflammatory response from the innate and adaptive immune system. The destruction of the periodontium allows for bacteria and bacterial products to gain access to the systemic circulation through the ulcerated epithelium and destruction of the periodontium.

However, there are evidences regarding the risk of PCOS patients to develop periodontitis and vice-versa, in a potential bidirectional relationship, and the potential role of PCOS associated inflammation on periodontal tissue health.[3]

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Clinical features and diagnosis of polycystic ovary syndrome

PCOS is a complex, heterogeneous endocrine disorder, characterized by the presence of menstrual abnormalities (oligomenorrhea or amenorrhea), oligo-ovulation, hyperandrogenism and ultrasound findings. It usually affects women in their reproductive years.[4] It was first reported in the modern medical literature by Stein and Leventhal, in 1935, who in their original report described PCOS as a variable clinical condition with characteristics such as obesity, hirsutism, acne, and amenorrhea associated with enlarged bilateral polycystic ovaries. Later in 1990, at an international meeting which was held at the U. S. National Institutes of Health, it was recommended that the diagnostic criteria for PCOS should comprisethe concomitant presence of anovulation and evidence of hyperandrogenemia. The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group suggested that if two of the three criteria (CA, hyperandrogenism, and polycystic ovaries on ultrasonography) were present, it can be considered as PCOS. In contrast, the Androgen Excess Society states that hyperandrogenism is the key feature and its presence in combination with ovarian dysfunction is considered during the diagnosis of PCOS. The criteria mentioned in table I are considered in the diagnosis of PCOS, and to confirm this syndrome, diseases with similar clinical characteristics of PCOS must be excluded, such as thyroid disorders, hyperprolactinemia, and nonclassical congenital adrenal hyperplasia.[5]

Etiology and pathophysiology of polycystic ovary syndrome

The etiology and pathophysiology of PCOS are complex and are the results of interaction between genetic, metabolic, fetal, and environmental factors. Research suggests that the disease is originated in the intrauterine environment, indicating the importance of genetic factors. However, Franks and Berga et al. indicated that genetic factors play only a partial role in the etiology of PCOS. Abbott et al. suggested that the clinical features of PCOS may develop as a consequence of genetically determined hypersecretion of androgens by the ovary. It might also have an association with many other factors, such as socioeconomic conditions, ethnic factors, diet, physical activity, and lifestyle. The following are some of the pathophysiological mechanisms of PCOS, suggested by King:

- ❖ Altered secretion of the gonadotropin-releasing hormone
- ❖ Defect in androgen synthesis
- ❖ Development of insulin resistance(IR)

One of the best-described theories to explain the pathogenesis of PCOS is the disturbance of the hypothalamic-pituitary axis, resulting in disordered secretion of gonadotropin by the hypothalamus leading to raised luteinizing hormone (LH) levels and normal or low follicle-stimulating hormone (FSH) levels.[6]

According to Qiao and Feng,deficient FSH, excess secretion of LH, hyperandrogenemia of ovarian or adrenal origin, and hyperinsulinemia with IR are the extraovarian factors for PCOS pathogenesis, and the

Table I: Criteria for the diagnosis of polycystic ovary syndrome

NIH/NICHD, 1992[23]	Rotterdam criteria, 2004[20]	Androgen Excess Society, 2006[24]
Includes all the following	Includes two of the following	Includes all the following
Hyperandrogenism and/or hyperandrogenemia	Clinical and/or biochemical hyperandrogenism	Clinical and/or biochemical hyperandrogenism
Oligo- ovulation/anovulationn	Oligo-ovulation or anovulation polycystic ovaries	Ovarian dysfunction and/or polycystic ovaries

intraovarian factors could be raised levels of androgens that adversely affect follicular development, ovarian development, and meiotic maturation.[6]

Association of polycystic ovary syndrome with periodontal diseases

More recent studies showed significant associations between periodontal health and PCOS. The mechanisms that link these two disease entities are not completely and clearly understood but involve various aspects of inflammation. Hence, few authors reviewed various mechanisms that links PCOS and periodontal disease.

➢ Pathogenic mechanisms linking polycystic ovary syndrome and periodontitis:

PCOS is associated with low-grade systemic inflammation and is indicated by elevation of multiple markers of inflammation such as C-reactive protein (CRP), proinflammatory cytokines and chemokines including interleukin 18 (IL-18), monocyte chemoattractant protein-1 and macrophage inflammatory protein-1, and white blood count. Furthermore, increased oxidative stress and its biomarkers suggest PCOS as an inflammatory disease.

It is a deep-rooted fact that periodontitis is a chronic inflammatory disease and it is the inflammation that links periodontitis with various systemic diseases. Some inflammatory cytokines such as tumor necrosis factor α (TNF-α), IL-1 β, IL-6, leptin, adiponectin, and resistin and signaling pathways such as (IKKβ/NF-κB) Inhibitor of nuclear factor kappa-B kinase sub unit beta/Nuclear Transcription factor kappa-B pathway, c-Jun N-terminal kinase (JNK) pathway, and inflammasome pathway, link low-grade inflammation to IR, an important feature of PCOS.

- TNF-α triggers IR in visceral adipocytes by activating JNK1/2. IL-1β contributes to IR by impairing insulin signaling in peripheral tissues and macrophages, which leads to the reduced insulin sensitivity of β-cells and possible impaired insulin secretion.
- IL-6 causes IR by reducing the expression of glucose transporter-4 (GLUT-4) and insulin receptor substrate-1 (IRS-1) and by blocking the phosphoinositide 3-kinase (PI3K) pathway. IL-6 is considered as hormonally regulated, that stimulates the hypothalamic– pituitary–adrenal axis during inflammatory stress, and increased levels of IL-6 are correlated with obesity and IR, which are attributes of PCOS.
- CRP is one of the important markers of inflammation, produced under the stimulatory control of proinflammatory cytokines such as IL-6 and TNF-α. The raised CRP levels are observed in many systemic diseases, including PCOS, which is connected to low-grade chronic inflammation, linked to IR, that plays a critical role in syndrome pathogenesis along with hyperinsulinemia. Patients with periodontitis have a higher serum CRP levels and proinflammatory cytokines such as TNF-α and IL-1 in serum and/or gingival crevicular fluid (GCF).[7]

The elevated serum levels of CRP and other proinflammatory conditions, in chronic infections such as periodontitis, might induce systemic inflammation and oxidative stress leading to IR, which are characteristics of PCOS.

- Increased concentrations of inflammatory biomarkers such as CRP and IL-6 in both gingival tissue and serum have been found in patients with periodontitis.
- The argument that systemic inflammation is a pathophysiologic link between PCOS and periodontitis is reinforced by many epidemiological studies. A recent case–control study conducted by Rahiminejad et al. showed a higher prevalence of periodontal disease parameters in nonobese women with PCOS compared to systemically healthy controls and proposed that systemic inflammation could be the attributing factor.[7]
- In a cross-sectional study conducted by Porwal et al., a higher prevalence of periodontitis is found in patients who are newly diagnosed with PCOS than those on medical treatment for PCOS and systemically healthy females.
- Individuals with cytokines IL-17 A and IL-17F levels, were found to be higher in GCF and serum of chronic periodontitis and aggressive periodontitis patients, respectively, compared to healthy individuals.[7]
- Ozcaka et al.indicated a positive correlation between GCF IL-17A and serum IL-17A and IL-17A/F with clinical periodontal parameters in females with PCOS; similarly, higher serum, saliva, and GCF IL-6 levels were reported in patients with PCOS and

gingivitis compared with PCOS without gingivitis.[8]

- Akcalı et al. found that women with PCOS had raised serum and salivary MMP-8 concentrations, particularly in the presence of gingivitis and elevated MMP-8/TIMP-1 ratio in women with PCOS, irrespective of the presence of gingivitis.[9]
- WBC count is also a marker of low-grade inflammation and it is associated with many chronic inflammatory conditions. Orio et al. in a case–control study suggested that women with PCOS showed higher leukocyte count, a marker of low-grade inflammation and cardiovascular risk, than age- and body mass index-matched controls. Similarly, raised white blood cell count can be observed in chronic periodontitis patients.[9]

In the light of above-mentioned components of inflammation, as potential links between PCOS and periodontal disease, inflammation can be contemplated as a pathophysiologic mechanism operating behind the association between these two disorders.[7-9]

Gingival inflammation in patients with polycystic ovary syndrome

Elevated serum MMP-9 levels were observed in the presence of gingivitis in women with PCOS, whereas the reverse trend was the case for systemically healthy women. PCOS had a positive effect on MPO serum levels only in the presence of gingival inflammation. When it comes to the circulating levels of these enzymes this trend is better seen in PCOS group which seems to be more associated with the presence of this systemic condition. PCOS appears to cause an impairment of the physiological response of local and systemic MMP-9 and MPO levels, perplexed further by the presence of gingival inflammation.

MMPs are involved in ovarian follicle development and ovulation. The harmony between MMPs and their inhibitor is thought to reflect the condition of the proteolytic process. It has been previously speculated that increased gelatinolytic activity could be the explanation of the impaired ovarian function. PCOS did not seem to influence local levels of proteinases, circulating levels were affected with elevated levels of MMP-9 and MPO in the PCOS with gingivitis. Moreover, the proteolytic activation might be mediated by microbial proteases, other MMPs and MPO, but will probably be inhibited by TIMP-1. MPO can oxidatively not only activate MMP-9 but also inactivate TIMP-1.

Neutrophils also play a crucial role in the initiation of inflammatory response, by migrating through junctional epithelium into the gingival sulcus. As for the pathogenesis of the gingivitis, neutrophils handle the phagocytosis and neutralization of the bacteria that are about to invade the tissue. However, their aberrant stimulation can lead to the secretion of inflammatory products, including the associated proteinases, with destructive outcomes for the tissue. There is strong evidence on the correlation between MPO levels and periodontal diseases. MMP-8 and MMP-9 can thus activated by NE, MPO, and cytokines at the local site of inflammation. Higher levels of these enzymes have been reported in the saliva of patients with chronic and aggressive periodontitis. Increased levels of serum MMP-9 in patients with PCOS and gingivitis group might indicate a potentiated effect of gingival inflammation in PCOS.[10-12]

Bidirectional association between polycystic ovarian syndrome and periodontitis

The chances of PCOS increases by 28% for individuals having PD and in the same fashion, PD increases by 46% for individuals having PCOS. This bidirectional association demands further studies because we were only able to infer how the presence of PCOS links with some periodontal characteristics (such as gingival inflammation and periodontal structure loss), rather than ascribe how the variation of the PD condition influences PCOS clinical characteristics. PCOS females with PD had higher gingival inflammation and periodontal structure loss than non-PCOS females with PD. Individuals with PCOS also showed increased BOP, PPD and CAL. A persistent subclinical inflammation triggers the synthesis of a panel of proinflammatory markers (such as C-Reactive Protein (CRP), tumor necrosis factor-α, interleukin (IL)-6, IL-17, and matrix metalloproteinase-9) and potentiates an oxidative stress environment (through local oxidant status-like myeloperoxidase and nitric oxide). Further investigations on inflammation explains the biological mechanisms connecting these two entities. Additionally, PD management has been implicated in insulin levels control with periodontal treatment allowing

the alleviation of high glycemic levels, and therefore uncontrolled periodontitis may indirectly impact on PCOS clinical status.[13-14]

Conclusion

Considering above-discussed literature, we can excogitate that PCOS might exacerbate the periodontal condition that is caused by plaque, through various pathophysiological links, namely, low-grade systemic inflammation, oxidative stress, IR, AGE products, and systemic hormonal levels. Evidence has suggested that periodontal disease causes chronic subclinical inflammation leading to IR, initiating the development of type 2 diabetes, which is a prominent feature in PCOS. Hence, we can contemplate that there exists a two-way relationship between PCOS and periodontal disease. However, evidence linking the two is in its nascent stage and warrants further research. Multicenter studies with larger sample sizes and long terms are to be conducted to establish a clear and stronger association between the two disease entities and help in early diagnosis, treatment, and prevention of long-term sequelae. Health-care professionals, gynecologists, and endocrinologists in particular would need to proactively motivate patients diagnosed with PCOS to maintain good oral hygiene at all times and refer to dentist to avoid periodontal implications as this hormonal disorder can worsen the vulnerability to plaque-induced periodontal disease.

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Melanin v/s non melanin gingival pigmentation - A review

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ABSTRACT

The colour of the gingiva is an integral part in the overall esthetic appearance of an individual. Pigmentation is a discoloration of the oral mucosa or gingiva due to various conditions. Most of the pigmentation is physiologic but sometimes it can be a precursor of severe diseases. Melanin pigment irregularities and color changes of the oral tissues could provide significant diagnostic evidence of both local and systemic disease. This article aims at reviewing briefly about melanin synthesis and classification, etiology and treatment of gingival pigmentation.

Key Words: gingival pigmentation, melanin, melanocytes, gingiva, depigmentation

Introduction

The color of the gingiva is an integral part in the overall esthetic appearance of an individual. Pigmentation has multifactorial etiology. Pigmentation can be normal and abnormal discoloration of oral mucous membrane. Most of the pigmentation is physiologic but sometimes it can be a precursor of severe diseases. Melanin pigment irregularities and color changes of the oral tissues could provide significant diagnostic evidence of both local and systemic disease. Melanin, carotene, reduced haemoglobin and oxy-haemoglobin are the prime pigments contributing to the normal colour of the gingiva, out of which melanin shows the maximum incidence rate.[1] Excessive deposition of melanin located in the basal and supra-basal cell layers of the epithelium will result in gingival hyperpigmentation.[2] The name "melanin" comes from the Greek word "melanos", meaning "dark," and the term was first applied by the Swedish chemist Berzelius in 1840 to call a dark pigment extracted from eye membranes.[2]

Physiology of melanin pigmentation

The gingival color depends primarily upon

- The number and size of vasculature
- Epithelial thickness
- Degree of keratinization within the gingival epithelium

Melanin is the end-product of complex multistep transformations of L-tyrosine, are polymorphous and multifunctional biopolymers, represented by[3]

- Eumelanin
- Pheomelanin
- Neuromelanin

Melanocytes

Melanocytes constitute a heterogeneous group of cells. These unicellular dendritic cells reside in the basal cell layer of the epidermis and oral epithelium. Primitive melanocytes originate from neural crest of ectoderm. Melanocytes have a round nucleus with a

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double nucleus membrane and clear cytoplasm lacking desmosomes or attachment plates, but possess long dendritic processes[4].

Melanosomes

Melanocytes synthesize melanin in organelles called melanosomes. There are four stages in melanosome development[5]

Stage I Premelanosomes: They are round, small vesicles with an amorphous matrix.

Stage II Melanosomes: They have an organized, structured fibrillar matrix and tyrosinase is present but pigment synthesis has not been noted.

Stage III: The beginning of melanin production takes place at this stage, where pigment is deposited on protein fibrils.

Stage IV: At the last, pigment fills the whole melanosome.

Fully melanized melanosomes lose tyrosinase activity and are transported to surrounding keratinocytes by elements of the cytoskeletal system.

Melanoid

Melanoids are granules of melanoid pigment and are scattered in the stratum lucidum and stratum corneum of the skin. Melanoid imparts a clear yellow shade to the skin.

Melanogenesis

Melanin is synthesized by a process called melanogenesis. It takes place in cytoplasmic organelles called melanosomes of melanocytes. As a result two types of melanin are produced – pheomelanin and eumelanin. They differ in color and in the pathway of synthesis.[6]

The process of pigmentation

I) Activation of melanocytes: The activation phase occurs when the melanocytes are stimulated byfactors like stress hormones, sunlight etc. leading to production of chemical messengers like melanocyte stimulating hormone.

II) Synthesis of melanin: In synthesis phase, melanocytes make granules called melanosomes. This process occurs when the enzyme tyrosinase converts amino acid tyrosine into a molecule called dehydroxyphenylalanine (DOPA). Tyrosinase then converts DOPA into secondary chemical dopaquinone.After a series of reactions, dopaquinone is converted into either dark melanin (eumelanin) or light melanin (pheo-melanin).

III) Expression of melanin: In expression phase, melanosomes are transferred from the melanocytes to the keratinocytes which are the skin cells located above melanocytes in the epidermis. After this, melanin color eventually becomes visible on the surface of skin. Major determinant of normal human skin colour is the melanogenic activity within the melanocytes and the quantity and quality of melanin production, but not melanocyte density. The degree of clinical melanin pigmentation in human epidermis and in the epithelium of oral mucosa is related to the amount of melanin i.e. the maturation of melanosomes, the number of keratinocytes containing melanosomes and the distribution of melanin loaded keratinocytes throughout the epithelium[7].

Classification

Different classifications are used to classify pigmented lesions of the oral cavity.

1. Dummet *et al.* (1967)[8]

Primary oral melanin pigmentations

Secondary oral melanin pigmentations

Oral non-melanin pigmentations

Oral melanoclasias.

2. Brocheriou (1985)[9]

Non tumoral pigmentations

Non-melanin pigmented tumors or tumor-like lesions

Benign melanin pigmented tumors

Malignant melanomas

3. Meleti (2008)[10]

Melanin-associated lesions (e.g:- Racial pigmentations, melanotic macules, melanocytic nevi, and malignant melanoma).

Non melanin-associated lesions (e.g:- Blood-related pigmentations, metallic pigmentations).

4. Kauzman *et al.* (2004) classified pigmented lesions into different groups

Etiology of pigmentation

The causes of pigmentation is classified into two -Endogenous and Exogenous(Figure 1)

A. Endogenous pigmentation

1) Physiologic pigmentation or racial pigmentation

Oral pigmentation occurs in all races of man and it varies from one race to another. There are no significant differences in oral pigmentation between males and females. The intensity and distribution of racial pigmentation of the oral mucosa varies between the races, between different individuals of the same race and within different areas of the same mouth. Attached gingiva represents the most common intra-oral pigmented area. Other less common sites include hard palate, lips and tongue. Physiologic pigmentation develops during the first two decades of life but may not come to the patients notice until later. Color variation may be uniform, unilateral, bilateral, mottled, macular or blotched and may involve the gingival papillae alone or extend throughout the gingiva and into other oral tissues.

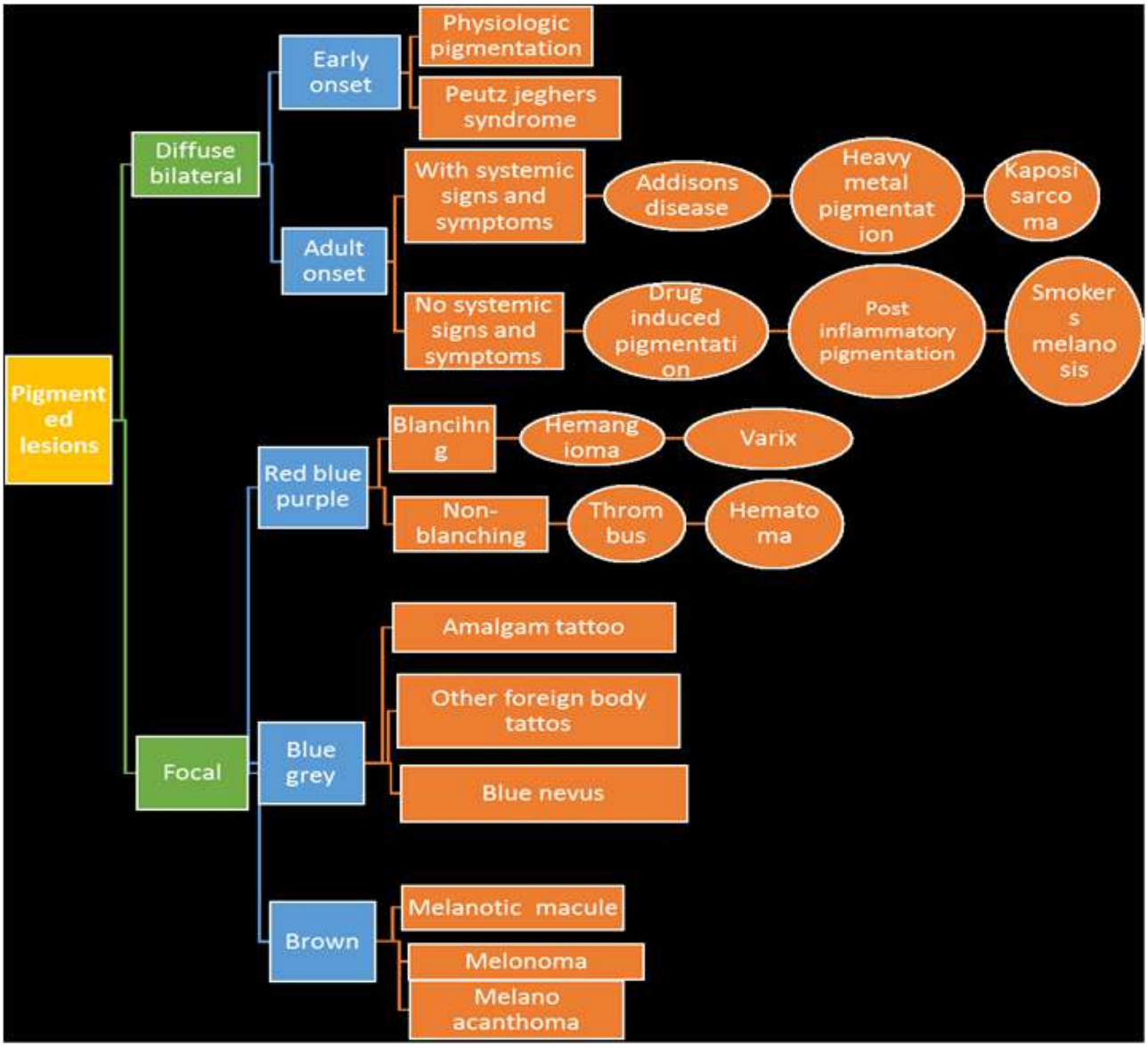

Figure 1: Ethiopathogenesis of pigmentation

2) Pathological pigmentation

I. Peutz-Jeghers syndrome

Peutz-Jeghers syndrome (intestinal polyposis) is a genetic disorder characterized by mucocutaneous pigmentation and hamartomas of the intestine. It manifests itself as freckle like macules about the hands, perioral skin, and intraorally to include the gingiva, buccal, and labial mucosa. Pigmented spots are particularly found on the lower lip and buccal mucosa but rarely on the upper lip, tongue, palate, and gingiva.

II. Addison's disease

Addison's disease, or primary hypoadrenalism, is due to progressive bilateral destruction of the adrenal cortex by autoimmune disease, infection or malignancy. The lack of adrenocortical hormones in the blood stimulates production of adrenocorticotropic hormone (ACTH) by the anterior pituitary gland. The increased production of ACTH induces melanocyte-stimulating hormone, which results in diffuse pigmentation of the skin and oral mucosa. Oral involvement presents as diffuse brown patches on the gingiva, buccal mucosa, palate and tongue, which may resemble physiologic pigmentation.

III. Kaposi's Sarcoma

Kaposi's sarcoma (KS) is a multifocal vascular malignancy seen predominantly in HIV-infected individuals. KS in the oral mucosa most commonly affects the hard palate, gingiva and the tongue.

IV. Post inflammatory pigmentation

Oral post-inflammatory pigmentation (OPP) is a discoloration of the oral mucosa caused by an excess of melanin production and deposition within the basal layer of the epithelium and connective tissue of areas affected by chronic inflammation. Clinically OPP appears as a localized or diffuse, black to brown pigmentation. OPP may persist for many years even though the disappearing of the pigmentation after the resolution of the inflammatory state has been reported.

V. Smoker's Melanosis

Smoking may cause oral pigmentation in light-skinned individuals and accentuate the pigmentation of dark skinned patients. There is increased production of melanin, which may provide a biologic defense against the noxious agents present in tobacco smoke. Smoker's melanosis occurs in up to 21.5% of smokers.

VI. Pigmented Nevi

Pigmented nevi of the oral cavity are uncommon. The clinical features include brownish black to blue elevated papules with a well-defined border. Nevi can be classified based on time of occurrence as congenital and acquired. Congenital nevi, can be sub-classified as giant nevus and small nevus. An acquired nevus is also called as a mole, occurs most commonly in the sun exposed regions. Nevus represents a benign proliferation of melanocytes.

VII. Oral Melanoacanthoma

Oral melanoacanthoma is an uncommon benign pigmented lesion of the oral mucosa characterized by proliferation of dendritic melanocytes scattered throughout the thickness of an acanthotic and hyperkeratotic surface epithelium.

VIII. Oral Melanoma

Oral mucosal melanoma is rare, accounting for less than 1% of all oral malignancies. It is characterized by proliferation of malignant melanocytes along the junction between the epithelial and connective tissues, as well as within the connective tissue. The most common site is the palate, which accounts for about 40% of cases, followed by the gingiva (30%), which accounts for one third of cases. Other oral mucosal sites may also be affected.

IX. HIV Infection

In patients infected with human immunodeficiency virus (HIV), progressive hyperpigmentation of the skin, oral mucosa, fingernails, and toenails have been reported being related to primary adrenocortical deficiency and to zidovudine (Azidothymidine) therapy in some cases. Clinically, oral pigmentation appears as irregular macules with brown or dark brown color. The tongue, buccal mucosa, and palate are the most commonly affected sites.

X. Laugier hunziker syndrome

LHS is an acquired, benign skin condition characterized by hyperpigmented macules on the lips and buccal mucosa associated with longitudinal melanonychia of nails. The buccal mucosa and the lips (usually the lower lip) are the most commonly involved sites, but gingiva, tongue, soft palate, and the hard palate can also be involved. The pigmentation is in the form of smooth-surfaced brown-, black-, or slate-colored macules measuring 1-5 mm in size.

XI. Hemangioma and Vascular Malformation

Hemangioma is a benign proliferation of the endothelial cells that line vascular channels. Vascular malformation is a structural anomaly of blood vessels without endothelial proliferation. Both lesions are developmental abnormalities, characterized by onset during infancy. Hemangioma regresses as the patient ages, but vascular malformation persists throughout life. The mouth, the tongue is the most common site of occurrence.

XII. Angiosarcoma

Angiosarcoma is a malignant mesenchymal tumor with a differentiation into vascular endothelium. In oral cavity involves lips, tongue, and floor of mouth, cheek and palate.

XII. Hereditary hemorrhagic telangiectasia (HHT)

Hereditary hemorrhagic telangiectasia (HHT) is an unusual bleeding disease which is clinically characterized by numerous angiomatous lesions (telangiectasia), hereditary incidence and hemorrhagic diathesis. The lesions generally involve the skin or mucous membranes (or both) and tend to bleed spontaneously after slight trauma. Overt lesions may be found on the lips, tongue, buccal mucosa,nasal mucosa; less common locations include ears, nail-beds, scalp; rare sites are the mucosa of the palate, the gingiva, and the remaining oral mucosa.

XIV. Haemochromatosis

Hemochromatosis is a chronic disease characterized by the deposition of excess iron (ferritin and hemosiderin) in the body tissues, resulting in fibrosis and functional insufficiency of the involved organs. Gingival or mucosal pigmentation is reported to occur in 15 to 25 per cent of patients with hemochromatosis.

XV. Ecchymosis

Ecchymosis commonly known as bruises, frequently occur after injury. Traumatic ecchymosis is common on the lips.

XVI. Petechiae

Petechiae are submucous or subcutaneous minute pinpoint hemorrhages. In most cases, the petechiae are identified on the soft palate, although any mucosal site may be affected.

B. Exogenous pigmentation

I. Heavy Metal Pigmentation

Increased levels of heavy metals (e.g., lead, bismuth, mercury, silver, arsenic and gold) in the blood represent a known cause of oral mucosal discolouration. In adults, the most common cause for such increased levels is occupational exposure to heavy metal vapours.. Lead results in bluish red or deep blue linear pigmentation of the gingival margin. Exposure to silver causes a violet marginal line, often accompanied by a diffuse bluish – grey discoloration throughout the oral mucosa.

II. Drugs associated with oral mucosal pigmentation

Mucosal discoloration associated with antimalarial like chloroquine is described as blue–grey or blue–black, and in most cases only the hard palate is involved. Laboratory studies have shown that these drugs may produce a direct stimulatory effect on the melanocytes.

Minocycline is a synthetic tetracycline used in the long term treatment of refractory acne vulgaris. It can cause pigmentation of the alveolar bone, which can be seen through the thin overlying oral mucosa (especially the maxillary anterior alveolar mucosa) as a grey discoloration. Minocycline has also been reported to cause pigmentation of the tongue.

A number of medications like Amiodarone, Amodioquine, Aziodiothymidine, chloroquine, Ketoconazole etc. may cause oral mucosal pigmentation.

The pathogenesis of drug-induced pigmentation depends upon the causative drug. It can involve accumulation of melanin, deposits of the drug or one of its metabolites, production of pigments under the influence of the drug or deposition of iron after damage to the dermal vessels.

III. Amalgam Tattoo

Amalgam tattoo is one of the most common causes of intraoral pigmentation, the etiology being embedded metallic silver. It presents clinically as a localized flat, blue–grey lesion of variable dimensions.

Amalgam may be introduced in several ways during restorative and surgical procedures:

1. It may be condensed in abraded gingiva during routine amalgam restorative work.

2. It may enter mucosa lacerated by rotary instruments during removal of old amalgam fillings or crown and bridge preparation of teeth with large amalgam restorations.

3. Broken pieces may be introduced into a socket or beneath the periosteum during extraction of teeth.

4. Particles may enter a surgical wound during root canal treatment with a retrograde amalgam filling. The gingiva and alveolar mucosa are the most common sites of involvement, but these lesions may also involve the floor of the mouth and the buccal mucosa and the mandibular region being affected more than the maxillary region.

IV. Graphite tattoo

Graphite may be noticed in the oral mucosa through accidental injury with a graphite pencil. The graphite tattoo occurs predominantly in women and youngsters from age 5 to 21 years. The size is variable, generally from 1 to 15 mm, and macules are blue-gray in color. Graphite tattoos occurs most frequently on the anterior palate of young children, appearing as an irregular grey to black macule. A history of injury confirms the diagnosis; otherwise, a biopsy should be performed to exclude the possibility of the other conditions. Graphite tattoos may be often confused with the more commonly seen amalgam tattoos. One differentiating factor may be the radiographic appearance of the lesion: whereas amalgam may (but not always) produce radio opacities near the area in question, graphite is radiolucent. Microscopically, the special stains can segregate the two.

Gingival depigmentation techniques

different procedures have been proposed for gingival depigmentation.Different gingival depigmentation methods are as follows

I. Methods used to remove the gingival pigmentation:

A. Surgical methods:

a. Scalpel surgical technique

b. Bur abrasion method

c. Electro-surgery

d. Cryosurgery,

e. Lasers,

f. Radiosurgery.

B. Chemical methods.

II. Methods used to mask the gingival pigmentation:

a. Free gingival graft.

b. Acellular dermal matrix allograft.

Scalpel surgical technique

In this technique, the pigmented gingival epithelium along with a layer of the underlying connective tissue is surgically removed by splitting the epithelium with blade. Care should be taken not to leave any pigmented remnants over the denuded area. It is known that the healing period for scalpel wounds is faster than other techniques. However, scalpel surgery causes bleeding during and after the procedure and it is necessary to cover the surgical site with periodontal dressing for 7-10 days. Though the initial results of depigmentation procedure are highly encouraging, there is a possibility of regimentation.

Bur abrasion method

In this technique a medium grit ball shaped diamond bur is used at high speeds to denude the epithelium. It is relatively simple, safe, non-aggressive method and easy to perform. Above all, it causes less discomfort and is esthetically acceptable to the patients.

Also, this technique does not require any sophisticated equipment and is hence, economical. On the other hand, bur abrasion method was found to be difficult in controlling the depth of de-epithelialization. Moreover, bleeding and post-operative pain are anticipated.

Electro-surgery

Electro-surgery is the use of high frequency electrical energy in the radio transmission frequency band, which is applied directly to tissue to induce histological effects. As the current passes, the impedance to the passage of current though the tissue generates heat, which boils the tissue water, creating steam, resulting in either cutting or coagulation of tissue. It was found that this method controls hemorrhage, permits adequate contouring of tissues, causes less discomfort to patient, less scar formation and lesser chair time, Electro-surgery requires more expertise than scalpel surgery. Prolonged or repeated application of current to tissue induces heat accumulation and undesired tissue destruction. Contact with periosteum or alveolar bone and vital teeth should be avoided.

Cryosurgery

In cryosurgery, the gingiva is freezed with different materials such as liquid nitrogen. This technique is based on rapid freezing of water and slow melting repeatedly, leading to tissue deterioration. The cryotherapy has some direct effects including cell dehydration, enzyme inhibition, protein denaturation, and cell death due to thermal shock. It has also some indirect effects such as changes in vasculature and immune response of the tissue, which leads to cell death. Regarding the advantages of this method, this technique is easy and rapid to apply, does not require anesthesia or suturing, and finally it does not cause any bleeding or scars. However, cryosurgery is followed by considerable swelling, and it is also accompanied by increased soft tissue destruction. Depth control is difficult, and optimal duration of freezing is not known, but prolonged freezing increases tissue destruction.

Lasers

Laser ablation of gingival depigmentation has been recognized as one of the effective, pleasant and reliable techniques. It is usually sufficient to eliminate the pigmented areas and do not require any periodontal dressing. It also shows reduced pain and discomfort due to formation of protein coagulum. Meanwhile, it allows clean and dryoperating field and stable results. Laser light may also seal free nerve endings. But it also has its own disadvantages of delayed wound healing, thermal damage, deep penetration and the comparably high costs of the procedure. Different lasers have been used for gingival depigmentation including carbon dioxide (10.600nm), diode (810nm), Neodymium: Yttrium Aluminium garnet (1.064nm) and Erbium: YAG (2.940nm) lasers. The diode laser has been introduced in dentistry few years back. It is a solid-state semiconductor laser that typically uses a combination of elements to change electrical energy into light energy. It also can be delivered through a flexible quartz fiber optic hand piece. This energy level is absorbed by pigmentation in the soft tissues and makes the diodelaser an excellent hemostatic agent. It also allows good visibility at the surgical site. The post-operative patient comfort is better at the surgical sites treated with diode laser than surgical scrapping method. The CO_2 laser causes minimal damage to the periosteum and boneunder the gingiva being treated, and it has the unique characteristic of being able to remove a thin layer of epithelium cleanly. YAG laser has demonstrated the best application of laser use, leaving the least thermal damage.

Radiosurgery

Radiosurgery describes the most advanced form of electro-surgery. It is the removal of soft tissue with the aid of radio frequency energy. This electromagnetic energy operates between the frequencies of 3.0 megahertz (MHz) to 4.0 MHz, with 4.0 MHz being the optimal frequency. The main advantage of radiosurgery can be found in its ability to produce coagulation in the operative area which would often have extensive bleeding. Also, some studies reported less thermal damage and faster healing with the 4 MHz radio wave technology over the scalpel and lasers. On the other hand, the main disadvantage of this method is that it requires at least two sittings for completion within 2 weeks of treatment.

Free gingival graft

Free Gingival Grafts are used to create a widened zone of attached gingiva and in root coverage procedures. It was described by Kumar et al, 2012 for treating severe physiologic melanin pigmentation requiring replacement with an unpigmented free gingival autograft. The result of this procedure showed no evidence of repigmentation even after 4.5 years. Of the 10 treated patients only 1 patient showed repigmentation after 1 year. Unfortunately, this technique is quite an invasive and an extensive procedure and has the disadvantage of a second surgical site (donor site), additional discomfort and poor tissue color matching at the recipient site.

Acellular dermal matrix allograft

After local anesthesia administration, two vertical incisions are performed on the non-pigmented tissue both mesial and distal to the pigmented area using a #15 scalpel blade. A horizontal sulcular incision is needed to reflect a partial thickness flap containing pigmented area and the reflected flap should be excised. The graft should be prepared and trimmed to fit the recipient site and secured to adjacent attached gingiva with sutures. This method is successfully used in the elimination or greater reduction of gingival melanin pigmentations, and is more efficient than epithelium abrasion after 12 months.

Conclusion

Gingival pigmentation though not a major complication, yet it greatly affects the facial appearance. The patient's medical history is important in determining its cause whether physiological or pathological, but the histopathological examination is conclusive. The recognition, identification, and clinical assessment of pigmentation is of great importance because of the possible risk of serious systemic disease, such as melanoma, various syndromes and the side effects of drugs. Accordingly, treatment of the pigmentation is determined either surgically or chemically.

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JSPIK

Nanotechnology in Periodontics – Big surprises in small packages?? A review

Anusree Raju[1], Sanjeev Raveendran[2], Shyamala Devi M.P[3]

ABSTRACT

With an ascending trend of regenerative treatments for periodontal diseases, scientists seek to develop techniques and materials to aid in the formation of new tissues to replace the damaged tissues. With the introduction of nanomaterials, periodontal therapy has been provided with a new horizon of treatment method. Recent nanotechnology advancements and innovations are increasingly providing a suitable solution for treatment of many disorders including periodontal diseases

Keywords: periodontitis, periodontal disease, nano-dentistry, nano robots

Introduction

Size does not define greatness, often surprises come in small packages and so is, Nanotechnology. It is a science that deal with physical and biochemical properties of materials and its constitutions at nanoscale dimensions.[1]

Nano came from a Greek word which means "dwarf." Concept of nanotechnology was brought into limelight by Late Richard Feynman a Nobel Prize winning physicist in a lecture titled, "There's plenty of room at the bottom" at the annual meeting held at American Physical Society, California Institute of Technology, Pasadena, CA. (1959). Norio Taniguchi (1974), defined the term nanotechnology as a technology consisting of the processing, separation, consolidation, and formation of material by one atom or one molecule.[2] A widely used definition for nanotechnology is "The creation and utilization of materials, devices, and systems through the control of matter on the nanometre scale (1-100 nm), i.e., at the level of atoms, molecules, and supramolecular structures.[3]

Nanomaterials are those materials with components less than 100 nm in at least one dimension, including clusters of atoms, grains less than 100 nm in size, fibres that are less than 100 nm diameter, films less than 100 nm in thickness, Nano holes, and composites that are a combination of these.[4]

Nanotechnology is not just the study of small things; it is the research and development of materials, devices, and systems exhibiting properties that are unique and different from those found on a larger scale. Thus, nanotechnology can be best described as a broad amalgamation of technologies from diverse fields such materials science, engineering, chemistry, biochemistry, medicine, and physics, each of which may have different characteristics and applications.[5] Recent nanotechnology advancement and innovations through Nano-dentistry are increasingly providing a suitable solution for the treatment of many dental disorders including periodontal disease.[6]

Nanotechnology is a promising technology that is playing an increasingly important role in the diagnostics, prognostics, prediction, and management of various treatments. While most research in this field is still in its infancy, there is widespread agreement that the findings may have an enormous impact on society,

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with the potential to improve the quality of human life. Although the achievement of the goal of complete regeneration of the periodontal tissues (cementum, periodontal ligament, and bone) for periodontal management was not possible for many years, recent developments in nanomaterials, and nanotechnology have provided a promising insight into the commercial applications of nanomaterials in the management of periodontal diseases.[7]

Historical Background

The use of nanoparticles began as early as 9th century for creating glittering pots in Mesopotamia. It was Richard. P. Feyman a noble laureate who gave the concept of nanotechnology. In 1974, Norio Taniguchi devised the term 'nanotechnology', then Professor Kerie. E. Drexler used the term nanotechnology separately and also gave the first guidelines in the field of nanotechnology. Nanotechnology came into application after the discovery of scanning tunnelling microscope by noble prize winners Binnig and Rohrer in 1986. In the wake of book by Drexler, Peterson and Pergamil in 1991 highlighting the facts on Nano robots and assemblers, the term Nanomedicine was introduced by R.A. Freitus in 2000. To enhance the research in this field "National Nanotechnology Initiative" was developed in 2000 by Michael Roco. During 2005 and 2010, various innovations in the field of 3D robotics, networking and active Nano products production were done and from 2011, the generation of subatomic nanotechnology has been in use.

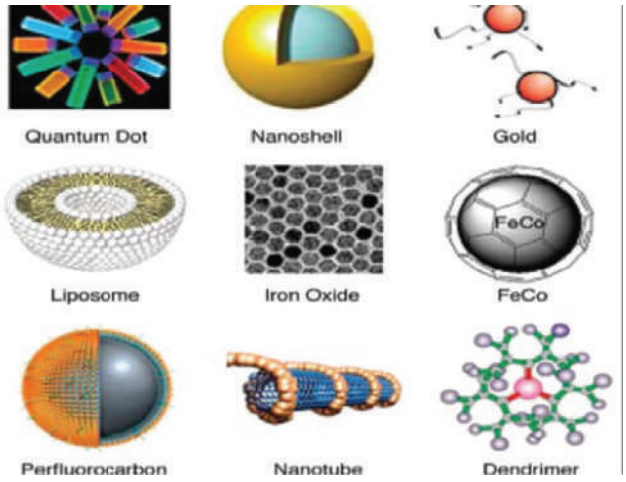

Figure 1: Different types of nanoparticles

Nanoparticles

Different types of nanoparticles are Nano pores, nanotubes, quantum dots, Nano shells, dendrimers, liposomes, Nano rods, fullerenes (Bucky-balls), Nano spheres, nanowires, Nano belts, Nano rings, Nano cap, and many more.[8]

Various types of nanoparticles being used for biomedical applications. Some of which are metallic, semiconductor and organic molecule nanomaterials with varieties of shapes, sizes, and structures.

How are nanoparticles made?

Different approaches for the synthesis of nanoparticles are top-down approach bottom-up approach and functional approach.[9] In top-down approach, particles are manufactured in the conventional manner and made smaller in size by grinding or milling. Examples of top-down approach are nanocomposites, Nano encapsulation, Nano needles, Nano based bone replacement cement, Nano impression materials, Nano coatings on implants. While in the bottom-up approach, nanoparticles are synthesized by direct molecular synthesis and bonding, i.e., they are synthesized from molecular level and assembled to form larger units.[10]

Properties of nanoparticles[11]

1. Better mechanical properties like enhanced toughness, stiffness, improved transparency, increased scratch, abrasion, solvent and heat resistance, and decreased gas permeability.

2. Nanoparticles have special properties, including chemical, optical, magnetic, and electro-optical properties, which differ from those of either individual molecules or bulk species.

3. They have significant surface effects, size effects, quantum effects and show better performance properties than traditional materials.

4. Important property of self-assembly by which they autonomously organize themselves into patterns or structures without any others intervention.

Applications of nanoparticles in periodontics

1. Dentin hypersensitivity: Dental Nano robots occlude specific dentinal tubules instantly. Besides they also render durable results. Nano hydroxyapatite

containing toothpastes are also shown to give promising results.[12]

2. Chronic periodontitis: Kadam et al hypothesized that adjunctive use of silver nanoparticle gel with scaling and root planning has superior effect in comparison to tetracycline gel in management of chronic periodontitis.[13] Nano Pro resolving lipid mediators because of their increased ability to penetrate into periodontitis affected tissue may be an effective method to manage chronic periodontitis. Recently, scientists produced and characterized triclosan loaded nanoparticles by the emulsification–diffusion process, in an attempt to obtain a novel delivery system adequate for the treatment of periodontal disease.[5]

3. Subgingival Irrigation: Hayakumo et al has described the use of ozone Nano bubble water produced by Nano bubble technology in subgingival irrigation. The results of their study demonstrated that it can be used as an adjunct to periodontal therapy because of their enhanced antibacterial activity.[14]

4. Biofilm management: Bioinspired Nano sized apatite's have been synthesized for modulation of bio-adhesion and biofilm management in the form of dentifrices, mouth rinsing solutions, and demineralizing pastes (fluids) for use in preventive dentistry.[15,16]

5. Nanorobotics Dentifrices[17]: Continuous removal supra and subgingival plaque and calculus through targeted Nano robots[1] sub occlusal-dwelling nanorobotics dentifrice delivered by mouthwash or toothpaste could patrol all supra-gingival and subgingival surfaces at least once a day, metabolizing trapped organic matter into harmless and odourless vapours and performing continuous calculus debridement. These invisibly small (1–10 m) dentifrice robots, perhaps numbering 103 × 105 Nano devices per oral cavity and crawling at 1–10 m/s, might have the mobility of tooth amoebas but would be purely inexpensive mechanical devices that would safely deactivate themselves if swallowed and would be programmed with strict occlusal avoidance protocols. Properly configured dentifrice robots could identify and destroy pathogenic bacteria residing in the plaque and elsewhere, while allowing the B500 species of harmless oral microflora to flourish in a healthy ecosystem. Dentifrice robots would also provide a continuous barrier to halitosis, since bacterial putrefaction is the central metabolic process involved in oral malodour.

6. Gingival surgical procedures: remarkable properties of TiO_2-based nanoparticles coupled with laser irradiation utilized in varieties of procedures such as depigmentation of gingiva, soft-tissue incision without anaesthesia and periodontal disease treatment.

7. Local drug delivery: Hollow spheres, core–shell structure, Nano tubules, and nanocomposite can be used as periodontal drug-delivery system.[5] Nanotechnology has proved itself as a potential frontier in drug delivery to specific cells or localized area of interest using nanoparticles.[1] Also, used to prevent bone loss in an experimental periodontal disease model by local application of nanostructured doxycycline gel.[17]

8. Self-assembling implants: C.X. Li et al investigated the effectiveness of nano structured self-assembling dental implants in type-II diabetes patients and stated that they exhibited decreased marginal bone loss and better Osseo integration than the conventional dental implants used.[18]

Conclusion

Nano dentistry is a multidisciplinary field of scientific research that highlights the application of new nanomaterials and devices in all the areas of human activity. Nanomaterials and Nano robots are of great interest when considering advances in nanotechnology. Although all the research activities for this promising field are at the initial stage, the results of the clinical studies have a strong potential to revolutionize the diagnosis and treatment planning as well as tissue regenerative materials for improving aesthetics in dental field. However more investigations and clinical trials are required for the application of nanotechnology in oral health and dental care.

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Soft tissue considerations in implant dentistry: An update

Preeja C[1], Arun Sivadas[2]

ABSTRACT

Dental implantology has provided us with one of the most promising tooth replacement procedures when placed into a proper and logical perspective and taking into account the periodontal considerations. An adequate band of attached gingiva and adequate vestibular depth can increase patient comfort, reduce the probability of gingival recession, enhance oral hygiene maintenance and simplify restorative procedures. In some cases where sub gingival margins are preferred, the margins should not be placed more than 0.5 mm into a healthy gingival sulcus. This facilitates oral hygiene and avoids encroachment on the biological width. Retraction of soft tissues for impressions is best accomplished with mechanical methods rather than lasers or electrosurgery. During restorative phase sound principles of crown contour, emergence profile and pontic design should be strictly followed for proper implant function. This article is oriented to describe all these periodontal dimensions that can enhance the prognosis of the dental implant.

Keywords: dental implants, periodontal considerations, biologic width, pontic design, emergence profile.

Introduction

A dental implant is a surgical component that interfaces with the bone of the jaw or skull to support a dental prosthesis such as a crown, bridge, denture, facial prosthesis or to act as an orthodontic anchor. There is a periodontal dimension in every dental restoration especially dental implants and we must empirically apply sound periodontal, surgical and restorative principles to the implant technique. This article gives an insight to those periodontal considerations that appear to enhance the prognosis of the dental implant.

1. Treatment planning for the implant patient

Accurate diagnosis complimented by a rational approach to treatment is necessary to achieve success in implant dentistry. To achieve this, a thorough medical and dental examination is required. The comprehensive dental examination helps to evaluate the patient's psychological attitude and to examine both clinically and radiographically the dental structures affected by the insertion of the dental implant and also quantity and quality of bone. Careful examination is done regarding the occlusal requirements, periodontal health and general condition of the existing teeth.[1-3]

2. Periodontal evaluation

The assessment of overall periodontal status is a crucial factor before planning an implant. The periodontal health of the existing teeth must be evaluated clinically as well as radiographically and their prognosis with adequate treatment and maintenance is determined. The periodontal tissues quickly reflect inadequacies in abutment selection, design of fixed and removable appliances, and the fit of these appliances.[2]

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All periodontal procedures affecting the implant site and adjacent or opposing natural teeth should be completed prior to the insertion of implant.

3. Mucogingival considerations

The health and stability of soft tissues surrounding an implant is an important factor determining the success of an implant. The most frequently encountered mucogingival problem at the time of examination and evaluation for implant placement is a shallow vestibule or inadequate width of attached gingiva. In cases where there is shallow vestibule, proper oral hygiene maintenance is not possible and effective cleansing of proximal surfaces of the abutment teeth-implant with other oral hygiene aids is also affected resulting in accumulation of food debris and bacterial plaque leading to inflammation of tissues. Adequate width of attached and keratinized gingivais important in maintaining health around the natural dentition and dental implants because attached gingiva serves as a firm, resilient soft tissue base, resistant to functional stress. Specifically, attached gingiva is needed to reduce the probability of gingival recession in areas of aesthetic margin of placement, to facilitate impressions, and in some cases, to increase patient comfort. The margins of some restorations must be extended slightly into the gingival sulcus to meet aesthetic or retentive demands. To minimize the probability of recession, the gingival tissues should be clinically healthy and should be of adequate width. The accuracy of subgingival impressions depends on exposure of tooth preparation margins. This is best achieved when the soft tissues can be gently and atraumatically retracted and allowed to rebound after these procedures. An adequate band of keratinized and attached gingiva will increase the probability of this tissue rebound.[1,2]

4. Biologic width and Margin of Placement

The gingival tissues must attach to the tooth coronal to the alveolar bone and is in general, 2-3 mm, and a healthy tooth surface is needed for this attachment. This gingival attachment is usually constant at all levels of probing depth, and has been termed the biological width (Fig.1). In implant hard and soft tissue surface around an implant demonstrates supporting bone in direct approximation to the implant surface without any intervening soft tissues (i.e., no periodontal ligament). A connective tissue zone is present above the level of bone with fibers running parallel to the implant surface and no inserting fibers. There is a long junctional epithelial attachment, a gingival/mucosal sulcus lined with sulcular epithelium, and oral gingival/mucosal epithelium (outer surface of soft tissue).

Encroachment on the biological width can lead to bacterial accumulation, inflammation, increased probing depths, gingival recession or a combination of these problems. In normal (2-3 mm), healthy sulci with adequate bands of gingiva, margins can be placed 0.5mm into the sulcus. In general subgingival margins should be considered a compromise and supragingival margins are preferred. Where aesthetics are not a concern supragingival margins are recommended. Several principles should be taken into consideration when subgingival margin placement is necessary. The marginal fit should be optimal as rough restorations or open margins lead to an accumulation of bacterial pathogens associated with inflammatory periodontal diseases. The margins of restorations should extend only slightly into the gingival sulcus to facilitate oral hygiene and avoids encroachment on the "biological width". The materials used for the restoration should be compatible with the soft tissues. In areas of aesthetic concern, the connection of the implant and the prosthetic element is located below the soft tissue margin. To minimize the effect of the bacterial trap at

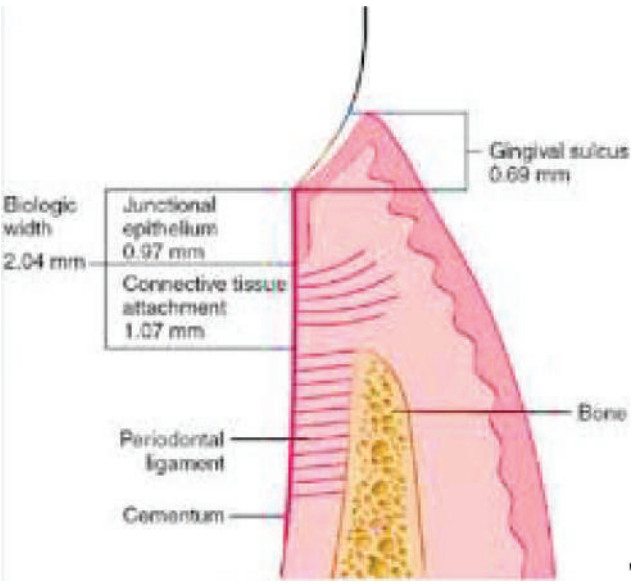

Fig.1: Biologic Width

this implant/restorative junction, the clinician should consider selection of an implant system that:

1) has this interface coronal to the facial and lingual bone,

2) provides the closest possible implant abutment interface, and

3) allows screw-retained restorations[1].

5. Modifications in Surgical Entry or Design of Flap

The main purpose of the implant surgery is to establish the anchorage for the future fixed prosthetic construction (Branemark et al 1985). In principle two different flap designs can be used, vestibular or crestal incisions. The surgeon should select the best method suited for the individual situation. Usually if the top of the crest is wider, it is more convenient to use a crestal incision. If the crest is high and narrow, a buccal approach might be better. For buccal approach, a horizontal incision is made within the attached gingival on the facial aspect of the edentulous ridge and Vertical releasing incisions are made at the mesial and distal extremities of this incision and are extended across the edentulous ridge and onto the lingual aspect (Fig. 2). A general recommendation when placing implants close to the teeth is to make the incision within the pocket region in order to get sufficient width of the mucosa for its nutrition and to obtain full mucosa coverage of the implant. But, whenever possible it is suggested that the gingival of the neighboring tooth be avoided, which gives a better esthetic result for the appearance of the soft tissue margin of teeth.

A full thickness mucoperiosteal flap is now reflected and alveolar bone is adequately exposed for the preparation of the trench into which the implant will be inserted. After placement of the implant the flaps are appropriately positioned and sutured.[1,5] Recently, an innovative technique of implant placement without elevating a mucoperiosteal flap described as flapless implant surgery has been introduced. It has the distinct advantage of reduced bone loss and increased patient comfort. It is a relatively new technique and literature lacks sufficient documentation for its credibility to be implemented in routine clinical practice.[3]

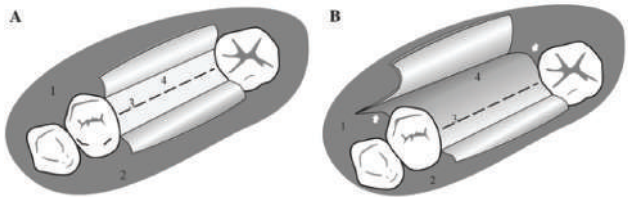

Fig.2: Flap design

6. Considerations in taking impression

The extension of preparations below the free gingival margin and the use of elastic impression materials necessitate the exposure of gingival margins of preparations to allow for their accurate duplication. Gingival retraction methods include gingival retraction cords, electrosurgery, laser tissue sculpting, copper bands etc. gingival retraction by retraction cords is the most widely used technique. There are different techniques including the single and double cord techniques. The use of bands as a displacement technique, whether with impression compound or elastic materials, is an accurate and effective method of gingival retraction. However, trimming and fitting of such bands must bed one with great care because excessive pressure or extension of the band may sever or traumatize the gingival attachment and lead to irreversible gingival recession.

Other methods include the use of electrosurgery or lasers but injudicious use of either of these instruments can cause excessive necrosis of the gingiva and,in extreme cases, the underlying bone. Also tissue resection has the potential of reducing soft tissue height and causing bone destruction. This may lead to exposure of margins or compromised aesthetics and respective procedures should be avoided in areas where the gingival architecture is thin[1,6].

7. Periodontal-restorative considerations

The restorative considerations in the rehabilitative phase of implant therapy and proper principles of crown contour, pontic design, and occlusion must be strictly followed for normal implant function.[6]

8. Crown Contour and Emergence Profile

Crown contours are normally determined by tooth anatomy, periodontal condition, margin placement, and access for oral hygiene. However, compromises must occasionally be made in the interest

of aesthetics or to reduce food impaction. Proper restorative contours require adequate tooth reduction to allow proper thickness of restorative materials, while allowing easy access for personal oral hygiene. The crown contour should be adequately tapered from the occlusal third to the cervical third so that the interproximal embrassure formedis of sufficient dimension thus promoting oral hygiene measures and improves the gingival health.[6,7] The emergence profile of a restoration in aesthetic areas has two aspects: subgingival form and supragingival form. The subgingival form should follow the contours of the cementoenamel junction and support the gingival tissues. Within limits, increased thickness of interproximal subgingival contours leads to increased papillary height, while increased facial contours lead to apical positioning of the gingival tissues.

9. Pontic Design

Pontic design is a key factor directly affecting the periodontal maintenance. Various designs for pontics have been suggested and specifications for the design of pontics which will enhance the periodontal maintenance of the fixed bridge and its adjacent structures have been recommended.

In an attempt to design a posterior pontic which is more easily maintained, Perel has recommended the use of a 'modified sanitary pontic' which makes food retention impossible, enhances oral hygiene and due to its architectural design, provides increased strength for the fixed bridge. In those areas where esthetics area concern the 'modified ridge lap pontic' for posterior segments and the 'lap-facing pontic' for anterior segments should be utilized. The disadvantage of ridge lap pontic is food impaction and plaque accumulation leading to gingival inflammation.

10. Maintenance of the Implant Prosthesis

The maintenance of the implant, its functioning prosthesis, surrounding periodontal tissues all should be done like that of the natural dentition. It is the patient's responsibility to practice meticulous oral hygiene measures for removal of bacterial plaque deposits. The dentist should call the patient for regular maintenance appointments, preferably every three months. During each recall a thorough evaluation of oral hygiene effectiveness is performed along with a thorough prophylaxis. Instead of metal curettes or ultrasonic instruments, plastic instruments should be used for prophylaxis. The occlusion should be evaluated for premature contacts. Routine radiographs should be taken and examined for any pathological change in the bone which supports or surrounds the implant. Any areas of suppuration or acute gingival inflammation should be treated in the same manner as the periodontal lesion involving a natural teeth i.e. curettage, debridement and antibiotics.[3,8]

Conclusion

Periodontal health should be thoroughly evaluated when planning for prosthetic rehabilitation of a patient's dentition. The periodontal tissues quickly reflect inadequacies in abutment selection, design of fixed and removable appliances, and the fit of these appliances. Also when inserted into a patient's mouth where active periodontal disease exists, it can affect the prognosis of the dental implant. When placed into a proper and logical perspective and taking into account the periodontal considerations and examining the clinical results implant dentistry can be accepted as a reliable and widely accepted procedure.

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Biomimetic coatings for Dental Implant: An update

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ABSTRACT

Dental implants have revolutionized the treatment of edentulous patients for the last two decades demonstrating high success and survival rates. Osseointegration, is considered as a pivotal process in dental implants and is affected by various factors, one among the important factor is surface characteristics. The modification of implants surface for better osseointegration has raised increasing attention in modern era and the use of biomimetic agents represents a growing area of research in implant dentistry. The implant surface coating with biomimetics may enhance the biocompatibility of the implant material, and fasten the osseointegration and also a shortened period of healing which is desirable for both the clinician and the patient thereby improve the patients quality of life. This paper provides an update on evidence based overview of biomimetic surface coatings such as bioactive bioceramics, Growth factors, Extracellular matrix Proteins, Peptides and Bioactive drugs on dental implants.

Keywords: osseointegration; biomimetic surface coatings; surface characteristics

Introduction

The successful replacement of lost natural tooth by means of tissue-integrated implants represents a major advance in clinical treatment.[1] Osseointegration is essentially required for the success of dental implants, where a direct contact and interface is essentially required between peri-implant tissues and implant surface without intervening the connective tissue layer. The pivotal factors for enhanced osseointegration are biocompatibility of the implant material, macroscopic and microscopic nature of the implant surface & designs, bone quality and quantity, undisturbed healing phase, the loading conditions and the implant finish.[2]

There is enhanced interest in the planning and advancement of implants to reduce failure and improve longevity. The use of micro-rough surface topography has increased the biomechanical properties of implant bone interface.[3] The surface properties of material are regarded as critical for tissue response with the material. Several strategies for improving the biocompatibility and osteogenic capacity of metal implants have been developed ranging from surface modification by inorganic mineral coatings, biocoatings of implant surface to control peri-implant tissue responses.[4] These surface modifications largely enhance the biocompatibility of the implant material, improve the adsorption of protein, cells and results in faster osseointegration and also a shortened period of healing which is desirable for both the clinician and the patient thereby improve the patients quality of life.[2] Hence the aim of this review is to present brief update on the various biomimetic coatings which is utilized to improve the surface characteristic of dental implants.

Implant surface modification

The Earliest dental implants of stone and ivory were reported in China and Egypt in the 16th and

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17th centuries. Also metal Implants of Gold, Lead, Iridium, Tantalum, stainless steel and cobalt alloy and a variety of polymers, including ultrahigh molecular weight polyurethane, polyamide, polymethyl methacrylate resin, polytetrafluoroethylene, and polyurethane, have been used as dental implant.[5] In the present era, advancements in the field of biomaterials pave the way to the emergence of newer implant materials such as zirconia, roxolid, surface modified titanium implants. These materials not only fulfill the functional requirements but are also esthetically blissful.[6]

In dental implants, surface roughness are often modified to modulate bone apposition. Surface roughness can be described as macro-, micro-, and nanometer-sized texture. Macro- and micrometer roughness facilitates mechanical anchorage to bone where as nanometer roughness affects the adsorption of proteins and the adhesion of osteoblastic cells.[7] A series of surface modifications has been developed and applied to produce the desired surface topography on implants by different subtracting and additive methods and biochemical (biomimetic and Antimicrobial coating methods).

Biomimetics in Dental implant: new ways to enhance osseointegration

Biomimetic dental implants are considered as the newer clinical trends in the field of implant surface modification. Otto Schmitt in 1950's coined the term "Biomimetics". It can be defined as the study of the structure, formation, and function of biologically produced materials and also biological mechanisms and processes for the purpose of synthesizing similar products by artificial mechanisms which mimic natural ones.[8] Thus the main principle of biomimetics in implant dentistry is to replace the lost dental tissues by materials to restore full function and bear with all functional stresses along with the maintenance of esthetic results.

Biomimetic agents applied to the implant surfaces should possess the following characteristics:[9]

(1) Ability to induce differentiation of the appropriate cells for enhancing new bone formation

(2) Easy synthesis or production, avoiding extraction from allografts to eliminate the risk of transmission of infectious-contagious diseases

(3) Resorbability in response to osteogenic action, avoiding problems of implant loss due to delamination of the coating

(4) No production of immune reactions in the receptor

(5) Chemical stability until placement of the implant in the surgical socket

(6) Good cost-effectiveness ratio.

Table 1: Methods of surface modification for dental implant

Physical/ substractive	Chemical / addictive	Biochemical	
		Biomimetic coating	Antimicrobial coating
1. Machined surface 2. Sandblast, large-grit, and acid etching (SLA) 3. Laser etching-shot / laser peening	1. Acid etching 2. Dual acid etching (DAE) 3. Anodic oxidation 4. Alkaline etch 5. TPS 6. Implants by sol gel 7. Vaccum treatment 8. Polymer demixing 9. Ion implantation Chemical vapor deposition 10. Flouride-modified implant surfaces 11. Photofunctionalization	*1. Bioceramics:* Bioactive calcium phosphates, Nanoreinforced bioceramics *2. Growth factors:* BMP, Rh-BMP, FGF, PDGF, VEGF, GDF, TGF *3. Extracellular matrix Proteins:* chondroitin sulfate, fibronectin, vitronectin *4. Peptides:* KRSR, RGD, PLL-g-PEG *5. Bioactive drugs:* Bisphosphonates drugs, Strontium ranelate, Statins, Vitamin D	1. Antibiotic Coating 2. Polysaccharide Antibacterial Coatings 3. Antimicrobial Peptides (AMPs) Coating 4. Antimicrobial Properties of Metal Element Components coating

Various types of biomimetic coatings in dental implant an evidence based review

1. Dental Implant surface coatings with Bioactive Bioceramics

Bioactive calcium phosphate ceramics as coatings on bioinert metallic substrate have received attention in dental implants due to their biocompatibility and their ability to bond directly to bone.[10] Implants coated with calcium phosphates, release the calcium and phosphate into peri-implant area and increase their saturation in the body fluid and precipitates the hydroxyapatite on the surface of dental implants.[11] This layer contains endogenous proteins and serve as a matrix for osteogenic cell attachment and growth. The bone healing process around the implant is therefore enhanced by this biological apatite layer.[12] Different methods have been developed to coat metal implants with calcium phosphates are: plasmaspraying, sputter-deposition, sol–gel coating, micro-arc oxidation, electrophoretic deposition or biomimetic precipitation. There are different forms of application of calcium phosphate such as Hydroxyapatite, Beta tricalcium phosphate. These forms are commonly used due to their osteoconductivity, crystallographic structures, and chemical composition similar to the skeletal tissue.[13]

Recently Nano-hydroxyapatite is used to enhance the implant surface properties, which could be combined with collagen, bioglass, or titanium dioxide in a composite way to simulate the bio-environment of native bones.[14] The nano-size particles strongly increases, their specific surface area and adsorption ability. Regardless of time, nano-hydroxyapatite coating provides more bone bonding with dental implants compared

Table 2 : Surface coatings of dental implants with Bioactive bioceramics-– Evidence based review

Author (Year)	Outcome
Cao et al. 2006[16]	In the in-vivo study it shows a successful osseointegration of hydroxyapatite coatings with surrounding bone tissue when a hydroxyapatite coated implant was placed within living bone.
Lin et al 2009[17]	DCD-derived surface modification with HA nanoparticles on titanium and Ti-6Al-4V implants resulted in progressive osseointegration profiles that were distinctively different from those of DAE controls.
UgoRipamonti et al 2012[18]	These data in non-human primates indicate that geometrically-constructed plasma-sprayed titanium implants are per se osteogenic, the concavities providing a unique microenvironment to initiate bone differentiation by induction.
H.S. Alghamdi et al 2013[19]	Radiofrequent magnetron-sputtered calcium phosphate coating demonstrated that, dental implant modification with a thin CaP coating effectively improves osseointegration in both healthy and osteoporotic conditions.
Jing et al 2015[20]	The HA coating by micro-arc oxidation approach can significantly promote bone ingrowth and the mechanical performance of the bone–implant interface.
A Carradò et al 2017[21]	Nanoporous hydroxyapatite/sodium titanate bilayer improves the in-vivo osteoconduction and osteointegration. It prevents the delamination during the screwing and it could increase HA-coated dental implant stability without adhesive failures.
Łukaszewska-Kuska M, et al 2018[22]	HA coating using a direct electrochemical method shows an potentially favorable chemical and physical characteristics fostering osseointegration.
Hu, Z et al 2019[23]	Ti-6Al-4V implants coated by the nanostructured HA could promote osteointegration by strengthening osteogenesis and angiogenesis, and further potentially target pathological bone loss in Diabetic Model
Fang, C et al 2019[24]	Nanocrystalline hydroxyapatites with SDF-1 perform excellent biocompatibility and great capacity on bone regeneration in vivo.

[DCD- Discrete crystalline deposition, DAE- Dual acid etching, SDF-1-stromal cell-derived factor-1, CaP- calcium phosphate]

with normal dual acid-etched surface. The capability of HA coatings to immobilize proteins and growth factors via non-covalent interactions results in hybrid coatings that accelerate bone healing processes.[15]

2. Dental Implant surface coatings with Growth factors

Growth factors are biologically active polypeptide hormones, which affect the immune function as well as proliferation, chemotaxis and differentiation of cells from the epithelium, connective tissue and bone.[25] In the first phase of osseointegration, platelets degranulate and release specific growth factors which in turn initiates the second phase of osseointegration, the inflammatory phase. These factors comprise

Table 3: Surface coatings of dental implants with Growth factors – Evidence based review

Author (Year)	Outcome
Anitua et al 2006[28]	The whole surface of the PRGF-treated implants was covered by newly formed bone, whereas only the upper half was surrounded in control implants. Thus it can be concluded that PRGF can accelerate bone regeneration in artificial defects and improve the osseointegration of titanium dental implants.
Lan et al. 2007[29]	Significantly more percentage of marked bone adjacent to the implant surface with recombinant BMP-2 compared to the surface with out rhBMP-2 at both 4 and 8 weeks. Thus the results confirmed that rhBMP-2 improves the quantity and quality of implant-bone osseointegration.
Park et al.2009[30]	on histomorphometric analysis and the removal torque testthe percentage of bone-implant contact for FGF-FN fusion protein coated anodized implants was higher for about (36.91%) than control group (29.47%).
Lee et al.2012[31]	Poly(lactide-coglycolide) (PLGA) in combination with bFGF coating on an anodized titanium implant surface by electrospray shows an enhance bone formation near the surface of an implant installed in bone.
Jong-Eun Kim et al 2013[32]	Anodized implants coated with rhBMP-2 and rhBMP - 2 + rhVEGF can induce vertical alveolar bone regeneration, but the combined effect of rhBMP-2 and rhVEGF was not verified.
Schliephake et al. 2015[33]	Implant surfaces with rhVEGF hybridization showed the highest Bone implant contact after implant placement.
Guang M et al 2017[34]	Coating the implant with VEGF in vivo experiments, could promote osteoblasts and endothelial cell expression.
DaeHyeok Yang et al 2017[35]	Adding both hBMP-2 and hGDF-5 to implant surface coating can improve the bone formation and osseointegration between host bone and the implant surface.
Al-Jarsha et al 2018[36]	The presentation of hBMP-7 adsorbed to titanium discs coated with poly(ethyl acrylate) (PEA) shows a more potent osteodifferentiation of the mesenchymal cells and maximize osseointegration by creating a specifical delivery system consisted of poly (ethyl acrylate) and very low concentration of BMP-7.
H. Gencay Keceli et al 2020[37]	After successful anodization and loading of PDGF and BMP-6 to the titanium implant revealed a high potential for an improved early osseointegration period by means of a better factor release curve and contribution to the osteoblastic cell proliferation, mineralization, and associated gene expression..

[PRGF - scaffold-like preparation rich in growth factors, rhBMP-2 -recombinant bone morphogenetic factor-2, FGF-FN-fibroblast growth factor-fibronectin. VEGF- Vascular endothelial growth factor, rhVEGF- recombinant Vascular endothelial growth factor, hBMP-2- human bone morphogenetic factor-2, hGDF - human Growth Differentiation Factor, PDGF- platelet-derived growth factor, BMP-6- bone morphogenetic factor-6]

platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), and fibroblast growth factor (FGF).[26] Macrophages are the second important source of growth factors. During the elimination of cell detritus, these cells release VEGF (vascular endothelial growth factor), PDGF, and FGF to initiate the proliferative phase of osseointegration. VEGF induces neoangiogenesis that is crucial for osteogenesis.[26]

More promising results are obtained from Bone morphogenetic proteins which have a biologically high potential for osteoinduction. BMPs belong to the transforming growth factor-(TGF-) superfamily.[27] BMP-2 and BMP-7 have been the most widely studied. Over the last decade, To acquire an adequate yield of BMPs recombinant BMP-2 and BMP-7 has been studied as a bone-modulating agent in implant dentistry.

Table 4 : Surface coatings of dental implants with Extracellular Matrix Proteins— Evidence based review

Author (Year)	Outcome
Stadlinger et al. 2008[40]	Implant surfaces coated with collagen and chondroitin sulfate (coll/CS) and collagen and chondroitin sulfate and BMP4 (coll/CS/BMP4) could lead to a higher degree of bone formation compared to other ECM components.[collagen (coll); collagen and decorin (coll/DC), coll/DC and TGF-β1, coll/CS/DC, TGF-β1 and BMP-4].
Morra et al. 2010[41]	Results suggest that surface immobilization of fibrillar collagen type I on acid etched Ti implant surfaces affects both in vitro response of bone cells and in vivo periimplant bone formation.
Alghamdi et al. et al 2013[42]	Nano-CaP and collagen-coated implants demonstrated a significantly higher BV in the inner zone compared to non-coated implants at 4 weeks. However, no significant difference was identified in the BV between all groups at 12 weeks as indicated by both histomorphometric and micro-CT analysis. It was concluded that collagen modification of implant surfaces did not improve periimplant bone formation.
Lee et al. 2014[43]	The results on histomorphometric analysis shows that, only the collagen + HA coating surfaces displayed significantly greater peri-implant bone formation and BIC. Furthermore, adding BMP-2 to the implant surface did not show any advantage compared to the collagen + HA coating surface.
Korn et al. 2014[44]	Study shows no significant difference in BIC 4 weeks after implant placement of collagen/chondroitin sulfate coated or collagen/sulfated hyaluronan coated implants compared to grit-blasted, acidetched implants.
de Barros et al. 2015[45]	Increase in bone volume and mineralization for collagen type II/chondroitin sulfate coated implants compared to uncoated controls.
Raphel, J et al 2016[46]	Elastin-like protein (ELP) coatings on the titanium-base implants rapidly promote osseointegration, enable titanium implants to load force at an early stage, and to some extent prevent the micromotion possibly related to aseptic loosening.
Yin, D et al 2019[47]	Found that mussel adhesive protein (MAP) which is biocompatible, biodegradable, and non-toxic, can be a potential titanium implant surface coating. Its physicochemical properties accelerate early cell adhesion and proliferation and promote osteogenic cell differentiation
Yu Wu et al 202048	Biomimetic titanium implants coated with mineralized extracellular matrix constructed by culturing bone marrow mesenchymal stromal cells shows an enhanced and accelerated osteogenesis of bone marrow stromal cells by increasing cell proliferation and calcium deposition.

[BIC-Bone implant contact, Nano-CaP- Nano-calcium phosphates, HA –Hydroxyapatite, BMP-2- bone morphogenetic factor-2]

3. Dental Implant surface coatings with Extracellular Matrix Proteins

Extracellular matrix (ECM) proteins onto the implant surfaces is another option to enhance the biocompatibility of dental implants, aiming to regulate cell-matrix adhesion. Most commonly studied extracellular matrix proteins are collagen, chondroitin sulfate, fibronectin, vitronectin, and other proteoglycans.[26] This ECM protein appears to play a major role in initial bone healing by reorganizing the intracellular microfilaments and microtubules, which facilitates cell attachment and spreading and serve as a guide for osteoprogenitor cell migration to the implant surface through the action of cell surface integrins and fibronectin arginine–glycine–asparginine (RGD) motifs.[38] However, the use of such an original protein has several critical limitations: a high cost for synthesis, antigenicity and instability of the molecule, and steric hindrance of this macromolecule in focal adhesion.[39]

Table 5: Surface coatings of dental implants with peptides-Evidence based review.

Author (Year)	Outcome
Yves Germanier et al 2006[51]	RGD-coated implants demonstrated significantly higher percentages of bone-to-implant contact as compared with controls (61.68% vs. 43.62%; Po0.001). It can be concluded that the (PLL-g-PEG/PEG–RGD) coatings may promote enhanced bone apposition during the early stages of bone regeneration.
Barros et al 2009[52]	The modified microstructured surface with a 'low concentration of the bioactive peptide' provided a higher adjacent bone density (54.6%) when compared to the other groups (microstructured + HA coating = 46.0%, microstructured only = 45.3% and microstructured + 'high concentration of the bioactive peptide' = 40.7%), but this difference was not statistically significant. Thus, the different concentrations of bioactive peptide lead to different results.
R Lutzet al 2010[53]	Biofunctionalization of the implant surface with a biomimetic active peptide (P-15) leads to significantly increased BIC rates at 14 and 30 days and higher peri-implant bone density at 30 days.
Broggini et al 2012[54]	BiofunctionalizingmodSLA surfaces with KRSR and RGD derivatives of PLL-g-PEG polymer does not increase BIC, bone fill, or interfacial shear strength.
Kang et al. 2013[55]	Titanium implants coated with a laminin-2-derived peptide can promote osseointegration by accelerating new bone formation in vivo.
petzold et al.2013[56]	Proline-rich synthetic peptide coated titanium implants have potential to promote osseointegration and bone healing in rabbit models.
Warnke, P.H et al 2013[57]	HBDs have a protective immune response and help to facilitate the bone remodeling according to the report.
Zhou et al 2015[58]	GL13K peptides conjugation onto the titanium microgroove proved the improved antibacterial cytocompatibility and promoted the cell growth in the microgrooves
Ardura et al 2016[59]	Local delivery of parathyroid hormone-related protein such as PTHrP (1–37) or PTHrP (107–111) from a degradable implant is an attractive strategy to improve bone regeneration in aged and diabetic subjects.
Cho et al. 2019[60]	Human vitronectin-derived peptide, VnP-16 reinforces the osteogenic potential of an SLA titanium dental implant when this peptide is applied to the SLA surface.

[RGD-Arg-Gly-Asp tripeptide, VnP-16- vitronectin-derived peptide, SLA- sandblasted with large grits and acid etched, HBD-Humman beta defensin, KRSR- lysine-arginine-serine-arginine, RGD - arginine-glycine-aspartic acid, PLL-g-PEG- poly-L-lysine-graft-poly (ethylene glycol), BIC-Bone implant contact]

4. Dental Implant surface coatings with peptides

A functional peptide derived from the parent protein is a notable alternative, to overcome these limitations of extracellular proteins and maintaining the original biological activity. Peptides are biomolecules composed of short sequences of amino acids. They resemble fragments of larger proteins.[49] In addition, bioactive peptides have advantages over larger protein molecules due to their robustness and sterilizability. Particular peptides that facilitate cell adhesion in osseointegration or that exert antibacterial effects have been employed to design novel implant surfaces. The RGD peptide is an important sequence of extracellular matrix proteins that acts as a binding site for integrin receptors in adhesion and migration of osteogenic cells.[50]

5. Bioactive drugs coated dental implants

New coating strategies to improve implant osseointegration involve the development of a dedicated drug-loading ability to locally target bone around dental implants more effectively.[61] Studies have demonstrated that antiresorptive (e.g., bisphosphonates) and anabolic (e.g., strontium ranelate, statins and Vitamin D) agents improve implant osseointegration in osteoporotic bone.

Bisphosphonates drugs: Commonly used bisphosphonate drugs (alendronate, etidronate, tiludronate, and zolendronate) act by stimulating osteoblasts and bone formation, and also inhibiting the osteoclastic activity and bone resorption.

Strontium ranelate and Statins: Strontium (Sr) is an

Table 6: Surface coating of dental implants with Bioactive drugs – Evidence based review

Author /Year	Outcome
Abtahi e t al 2012[65]	Thin, bisphosphonate-eluting fibrinogen coating might improve the fixation of metal implants in human bone thus it lead to new possibilities for orthopedic surgery in osteoporotic bone and for dental implants.
Nyan M et al 2015[66]	The porous film formed by MAO is favorable for adsorption of simvastatin and it has an early rapid release and this release could affect early cell response immediately after implantation.
Pura et al 2016[67]	Three-dimensional printed porous-coated cylindrical implants coated with three different doses (0.02, 0.06, and 0.18 mg/cm2) of alendronate revealed little to no effect on bone in growth compared with the HA-coated control implants.
Satue et al 2017[64]	Ti implants coated with UV-irradiated 7-DHC and Vit E promote in vivo gene expression of bone formation markers and ALP activity, while they keep their osteopromotive potential in vitro and composition when stored up to 12 weeks at 4°C.
Najeeb et al. 2017[68]	Bisphosphonate drugs (alendronate, pamidronate, and ibandronate) investigated for implant coatings in combination with other compounds (collagen, calcium phosphate, and chondroitin sulphate) showed a significant improvement in the bone formation
Shahrezaee M et al 2018[69]	Showed the beneficial effects of statins on upregulating bone morphogenetic protein-2 (BMP-2) in osteoblasts to treat osteoporosis. Local application of simvastatin is more effective in inducing bone formation as compared to systemic administration.
Panzavolta S et al 2018[70]	Sr-HA promotes proliferation and differentiation of osteoblasts in vitro and also shows good biocompatibility and osteoconductivity in - vivo.
Zhao et al 2020[71]	Simvastatin-strontium-hydroxyapatite coated implants perform in rabbits with osteoporosis exhibited marked improvements in osteointegration, which is characterized by a quicker mineralization deposition rate, good bone formation mode (large amount of contact osteogenesis and a small amount of distance osteogenesis) and increased bone-to-implant contact and pull-out strength.

[ALP- Alkaline phosthatase, 7-DHC-7-Dehydrocholesterol, MAO- micro arc oxidation, Sr-HA- strontium-containing hydroxyapatite]

essential trace element in the human body, which promote bone formation and inhibiting bone resorption. Strontium ranelate has been successfully used to treat osteoporosis. To minimize the adverse reactions of systemic administration, Sr can be introduced into HA matrix, due to the difference in the radii and properties of the two atoms, the lattice of Sr-doped HA can be distorted, the crystallinity and grain size of HA can decrease, and the biodegradability increases.[62] Statins, Studies have shown the beneficial effects of statins on upregulating bone morphogenetic protein-2 (BMP-2) in osteoblasts to treat osteoporosis. To enhance the action of statins they can be given locally rather than systemically.[63]

Vitamin D: vitamin D is a multifunctional hormone which avoid bone loss and maintain the structural integrity of the bone. vitamin D deficiency leads to decreased bone mineral density and increases the risk of fractures, were as its supplementation has shown beneficial effects on bone. Vitamin D3 at the surface of Ti implants produce active vitamin D by the cells, showing increased osteoblast differentiation on both osteoblastic and mesenchymal stem cells.[64]

Conclusion

Surface modified titanium implants shows a promising outcome in the field of implant dentistry. These surface adjustments resulted in the time effectiveness and prognosis of dental implants in different challenging clinical situations. Moreover, biomimetic agents onto implant surface, promote the osteogenetic process around implants, including inducing cell adherence, osteogenic stimulus, or even additional antibacterial effects. However,long-term clinical studies are still needed to compare performances of different coatings and assess success rates of novel implant-coating. In the future more optimized coating using modified technologies such as stem cells therapy and genetically engineered implant surfaces will be exploited for improving the performance of dental implants.

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Achievement

SPIK community congratulates **Dr. Baiju RM,** Addl Professor, Govt. Dental College, Kottayam on completing the prestigious FDS RCPS from the Royal College of Physicians and Surgeons (Glasgow).